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08-07-01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Applicant	:	William J. Schmidt
Serial No.	:	09/385,405
Filed	:	August 30, 1999
For	:	METHOD FOR THE PURIFICATION AND RECOVERY OF WASTE GELATIN
Examiner	:	R. Popovics
Art Unit	:	1723
Attorney Docket No.	:	671.1.002 CIP-3

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER OF PATENTS AND TRADEMARKS, WASHINGTON D.C. 20231
ON July 30, 2001
NAME Jill S. Garretson
SIGNATURE Jill S. Garretson

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

July 30, 2001

DECLARATION

Dear Sir:

I, William J. Schmidt, declare and say as follows:

1. I am the sole inventor of the subject matter of the present application. Furthermore, I am fully familiar with Schmidt, U.S. Patent No. 5,288,408 (hereinafter "the '408 Patent"), cited as a reference against the claims of the pending application, as I am one of the inventors of the '408 Patent.

2. I submit this Declaration and supporting documentation in support of the patentability of the claims of the pending application.

3. The '408 Patent discloses process technology for recovering gelatin and glycerin from a waste stream containing the same. The waste stream is dissolved in a solvent (e.g. deionized water) at a temperature of from 60 to 70°C and then diluted with deionized water to form an aqueous solution of gelatin and glycerin dispersed within the remaining oil and residual active-ingredient components ('408 Patent, column 3, lines 40-56).

4. The lower aqueous phase containing gelatin and glycerin is separated from the upper phase which typically contains lubricating or coating oils (e.g. mineral oil), active ingredients, coloring agents and preservatives (column 4, lines 9-13).

5. The lower phase (i.e. the aqueous phase) is hot filtered by the use of a plate filter, coated plate filter nutche filters or cartridge filters to remove any remaining trails of oil or other contaminants (column 4, lines 22-28) to form a filtrate.

6. The filtrate may then be concentrated by removing a portion of the water through the use of a vacuum distillation process (column 4, lines 32-63).

7. From the time of filing (October 26, 1992) of the patent application which led to the '408 Patent, I have personally observed that the process disclosed in the '408 Patent does not perform on a commercially acceptable scale when one or more of the

specific contaminants including oils with hydrophilic functioning groups (e.g. vitamin E acetate), aromatic oils such as fish oil and garlic oil, and suspended or particulate colorants such as titanium dioxide are present in the waste stream.

8. The present invention sought to improve upon the technology disclosed in the '408 Patent and was developed in response to commercial market criteria and the needs expressed by principal users of gelatin for the manufacture of soft gelatin capsules. In this regard, it was observed that a significant portion of waste gelatin produced commercially, especially in the soft gelatin capsule market contained material amounts of oils with hydrophilic functional groups, aromatic oils, and/or suspended particles.

9. The following tests are submitted to demonstrate the advantages of the present invention over what is fairly disclosed in the '408 Patent and were performed, coordinated and/or observed by me.

10. On or about December, 1998, the following test was performed at General Nutrition Products in Greenville, South Carolina. The test procedures and results are shown in Exhibit A herein. A waste gelatin stream containing gelatin, glycerin and vitamin E acetate (an oil with hydrophilic function groups) at a flow rate of 200 liters per minute at 50°C was treated in accordance with the '408 Patent by subjecting the aqueous phase, after separation from the non-aqueous phase, to treatment with a 10-μ polypropylene cartridge filter until a total of 140 kilograms of waste gelatin was treated. The resulting filtrate was then concentrated using ultra-filtration to obtain a

concentrated sample for analysis. Ultra-filtration was used for concentration because it was considered a more effective process for concentrating (i.e. dewatering) the filtrate than vacuum distillation as specifically disclosed in the '408 Patent.

11. The filtrate produced in accordance with paragraph 10 herein was observed to have a milky white appearance due to the presence of an unacceptable amount of residual emulsified oil. The resulting filtrate was deemed unsuitable for commercial scale recycling of gelatin.

12. On or about May, 2000, the following test was performed at Intergel, Division of IVC Industries in Irvington, New Jersey. The test procedures and results are shown in Exhibit B herein. A waste gelatin stream containing gelatin, glycerin and vitamin E acetate (an oil with hydrophilic function groups) at a flow rate of 200 liters per minute at 50°C was treated by subjecting the aqueous phase, after separation from the non-aqueous phase, to treatment with a 10-μ, polypropylene cartridge filter to produce a first filtrate. The first filtrate was then treated with a 0.65-μ tangential flow microfilter until a total of 145 kilograms of waste gelatin was treated. The resulting filtrate was then concentrated using ultra-filtration to obtain a concentrated sample for analysis.

13. The filtrate produced in accordance with Paragraph 12 herein was observed to have a clear, amber appearance typically associated with previous unprocessed gelatin. The microfiltration step employed in accordance with the present invention surprisingly eliminated residual emulsified oils to the extent that they were essentially undetectable in the resulting filtrate.

14. Soft gelatin capsules were successfully manufactured from the recovered gelatin product produced in accordance with Paragraph 12. In addition, a 3 month accelerated stability test was performed on the resulting capsules as compared with a control containing no recycled gelatin. The results showed no change in physical appearance compared to the control, no change in fill assay compared to the control, no change in microbiological parameters compared to the control, no change in dissolution profile compared to the control, a capsule strength and a seal strength equal to or exceeding the control, and adhesive properties equivalent to or better than the control (See Exhibit B).

15. On or about April, 1999 a series of tests similar to that described in Paragraphs 12-14 were performed at Pall Filtron Corporation, witnessed by representatives of General Nutrition Products and Intergel, with the exception that a 0.45-μ tangential flow microfilter was used to treat the waste gelatin instead of a 0.65-μ tangential flow microfilter. The results were very similar to that described in Paragraphs 12-14 herein, i.e the waste gelatin had a clear, amber appearance with essentially no detectable emulsified oils.

16. In October, 2000, large scale trials were performed at Nutricia Manufacturing USA, Inc. on behalf of Millipore Corporation (a licensee to Applicant herein) on a waste gelatin stream similar to that described in Paragraphs 10-14 to determine if a smaller pore cartridge filter in accordance with the '408 Patent could be effectively used to remove the residual emulsified oils. The test procedures and results are shown in Exhibit C herein. In this regard, a 1-μ and 0.3-μ cartridge filter were

tested. The 1-μ cartridge filter did not remove the residual oils. The 0.3-μ cartridge filter resulted in a reduced a unacceptable throughput and eventual oil breakthrough. Millipore's conclusion regarding this test was:

> "Due to low filtrate throughput and early breakthrough, the number of cartridges required for this application is very large and thus, the process becomes unrealistic."

17. In or about February, 2001, laboratory scale tests (900 ml batch size) were performed similar to the tests described in Paragraph 16 using a 0.5-μ cartridge filter at a reduced back pressure (i.e. 10 psig instead of 15 psig). The results showed very low throughput and oil breakthrough when the back pressure was increased. A 1-μ cartridge filter was used successfully on a laboratory scale at 10 psig but resulted in oil breakthrough when the batch size was increased from 900 ml to 120 l. It was thus clearly demonstrated by the test set forth in paragraphs 16 and 17, that cartridge filtration, as described in the '408 Patent, even with a smaller pore size, does not achieve the removal of contaminants achieved by the use of tangential flow microfitration as taught by the present invention. I consider this discovery to be surprising and unobvious from the '408 Patent disclosure.

18. In or about August, 2000 processes similar to that described in Paragraphs 10 and 12 respectively were conducted (See Exhibit D herein) on a waste gelatin stream containing gelatin, glycerin, and fish oil. In particular, a waste gelatin

stream (400 kg total batch) at a flow rate of 200 liters per minute at 50°C was treated with a 1-μ cartridge filter which resulted in a permeate having a distinct "fishy smell". When the process was carried out under the same conditions using a 1-μ cartridge filter and a 0.65-μ tangential flow microfilter, the permeate was odor free indicating that essentially all of the fish oil had been removed. The test procedures and successful results obtained in accordance with the present invention are shown in Exhibit D herein.

19. A waste stream containing suspended colorants such as titanium dioxide having an average particle size of 0.3-μ would require a cartridge filter having a pore size of about 0.1-μ. However, as discussed in paragraphs 16 and 17 herein, such small pore sizes would reduce the throughput of the waste stream to an extent that the process would be unacceptable on a commercial scale. Coated plate filters of the type described in the '408 Patent which typically have a pore size of 1-μ would allow the suspended particles to pass therethrough. Rosenmund and/or Nutche type filters are much too expensive to be practical for the commercial operation of treating waste streams containing suspended particles.

20. In accordance with the present invention, centrifugation which does not rely on pore size, has been successful in removing suspended particles form a waste gelatin stream containing the same.

21. I am aware that the Office Action states that the claimed invention is obvious in light of the '408 Patent. In addition to the comparative data presented herein, it is my view that the capsule manufacturing industry did not consider it obvious

to proceed from the technology disclosed in the '408 Patent to the technology claimed in the present application because the differences were not obvious. The industry did not make this transition despite an overwhelming need in the industry to effectively remove contaminants such as oils with hydrophobic functional groups from the waste stream. To further establish the non-obviousness of the claimed invention, I submit herewith a brief summary of the state of the capsule manufacturing from the time of the '408 Patent. In or about 1993, I made presentations and/or demonstrations, of the invention fairly disclosed in the '408 Patent, to soft gelatin capsule manufacturers including Pharmavite, Banner and R.P. Scherer, the latter two being the largest manufacturers of such capsules in the world.

From that time until the present application, no soft gelatin capsule manufacturer to my knowledge, including those highly reputable manufacturers mentioned above, made any advances in the field of waste stream recovery that resemble the present invention, despite their actual knowledge and exposure to the '408 Patent.

22. The nature of the waste gelatin problem addressed by the present invention is of such a magnitude that, if it were obvious to arrive at the present invention from the teachings of the '408 Patent, these leading soft gel manufacturers would have done so. Instead, I am in license negotiations with these companies, further indicating the need and non-obviousness of the present invention over the '408 Patent.

ARK:jsg072601/6711002CIP-3.DEC-WJS

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date:_____

_____
William J. Schmidt

Supporting Documentation For Paragraph 10 Of The Attached Response & Inventor Declaration

The '408' patent did not remove residual vitamin E acetate contamination, which has a hydrophilic functional group and partially emulsifies with water.

The December 1998 batch record enclosed in Section 1 herein employed the '408' patent with the modification of replacing vacuum distillation with tangential flow ultrafiltration.

The results were a milky process stream, from residual vitamin E acetate contamination, that could not be further processed into acceptable capsules.

The results of this experiment also verified that ultrafiltration could not remove residual oils as suggested by the Examiner.

How to address the issue of oily, hydrophilic contaminants was not obvious.

okay 11/30/98 WA

A.B. Technologies, L.L.C.

Pilot Manufacturing Directions **Revision Date: 11/28/98**
Gelatin Recovery **Revision: NEW**
Batch No: GNP
Clear - 25% recycle / 50kg gel mass → capsules

→ plus 20Kg for system hold-up (use separate ~~Rxn~~ vessel to pre-heat system)

- Charge 91.0Kg of deionized water for waste netting dissolution to a clean, previously inspected 33 gallon, stainless steel tank equipped with a hot water jacket and portable, variable speed agitator.

(1) Depth Structure Symetric Membrane Degasser
(2) After 2DV change to Asymmetric Degas Membrane

Agitation On yes RPM not measured

Kettle # 110

Deionized Water For Waste Netting Dissolution

	Charge #1	Charge #2	Charge #3	Charge #4	Charge #5	Charge #6
Gross Wt. (Kg)	24.06	24.46	24.32	22.96		
Tare Wt. (Kg) WA 12/1/98	~~1.58~~	1.58	1.58	0.00		
Net Wt. (Kg)	23.48	22.88	22.74	22.90		
Total Water Charged (Kg)	~~22.08~~	~~44.96~~	~~67.70~~	91.00		
	2248	4536	68.10			

- Heat the water to 45°C ± 2°C (113°F ± 4°F) with mild agitation. Maintain 45°C ± 2°C (113°F ± 4°F) throughout the manufacturing process.

Initial Temperature 70 °C, ____ °F Final Temperature ____ °C, ____ °F
Heating Start Time — Heating Stop Time — -s not required, pre-heated overnight

Agitation On yes RPM not measured

PROCESS NOTE: It is important to maintain 45°C ± 2°C (113°F ± 4°F) through the manufacturing process. Temperatures above 50°C (122°F) may result in degradation of the gelatin.

Date Processed: 12/1/98 **By:** [signature]

- When the water has reached 45°C ± 2°C (113°F ± 4°F), slowly add 23.4Kg of waste netting for dissolution while maintaining mild agitation.

Waste Netting For Dissolution

	Charge #1	Charge #2	Charge #3	Charge #4	Charge #5	Charge #6
Gross Wt. (Kg)	5.14	5.04	5.10	5.48	2.64	
Tare Wt. (Kg)	0	0	0	0	0	
Net Wt. (Kg)	5.14	5.04	5.10	5.48	2.64	
Total Netting Charged (Kg)	–				23.4	

Initial Temperature 65 °C, _____ °F Final Temperature 58 °C, _____ °F
Charge Start Time 8:35 Charge Stop Time 8:42

Netting Type Used Garlic

Agitation On YES RPM NOT MEASURED

PROCESS NOTE: A high agitation rate may result in the formation of a fine emulsion which is difficult to break and will not allow for efficient separation of the oil phase.

- Allow the netting to mix with mild agitation for 15 minutes until all the netting has dissolved. Use a plastic rod to check for complete dissolution of the waste netting. If dissolution is not complete, mix an additional 15 minutes with mild agitation. Repeat if necessary

Initial Temperature 58 °C, – °F Final Temperature – °C, _____ °F
Agitation Start Time 8:42 Agitation Stop Time 8:57
RPM NOT measured

Dissolution Complete ✓ YES (proceed to next step) _____ NO

~~Initial Temperature~~ _____ °C, _____ °F Final Temperature _____ °C, _____ °F
Agitation Start Time _____ Agitation Stop Time _____ RPM _____

Dissolution Complete _____ YES _____ NO

- Preheat the ultrafiltration unit to 45°C ± 2°C (113°F ± 4°F) by circulating hot water through the unit for 15 minutes. This will allow the ultrafiltration unit to be ready at the same time the separation is complete.

Initial Outlet Temperature ____°C, ____°F
Final Outlet Temperature 45°C, ____°F → pre-heated prior to dissolution - system holds temp well

Circulation Start Time — Circulation Stop Time —

PROCESS NOTE: It is important to preheat the diafiltration unit to avoid potential congealing of the aqueous gelatin layer being transferred.

- When dissolution of the waste netting is complete, stop agitation and allow the mixture to stand for 30 minutes.

Agitation Off ✓ YES

Hold Start 8:57 Hold Stop 9:27

- Transfer the lower, aqueous phase by means of a pump, through a sight glass to a clean, tared, 33 gallon, pre-heated stainless steel tank equipped with a hot water jacket, with hot water flowing through the jacket prior to the transfer, until the interface is observed in the sight glass at which time the transfer is complete. Maintain 45°C ± 2°C (113°F ± 4°F) in the transfer tank.

Tank # 117

Tank Pre-heated ✓ YES

Tank Tare Weight 103.8 Kg

Pre-Transfer Temperature 56 °C, _____ °F
Post-Transfer Temperature 54 °C, _____ °F

Transfer Start 9:40 Transfer Finished 9:48

Aqueous Phase Wt. 109.6 Kg

G - 213.4
T - 103.8
N 109.6

PROCESS NOTE: It is important to preheat the transfer tank to avoid potential congealing of the aqueous gelatin layer being transferred.

* a very thin small qty oil film observed after transfe

PROCESS NOTE: It is important to stop the separation as soon as the upper, oil phase is observed. Contamination of the aqueous layer with oil will result in cloudy capsules.

A.B. Technologies, L.L.C.

Pilot Manufacturing Directions
Gelatin Recovery
Batch No: GNP

Revision Date: 11/28/98
Revision: NEW

water 0.1

- Collect the upper oil layer, after removing/discarding the last of the aqueous layer in a suitable, clean container

G =
T = 1.12 1.60
N =

Oil Layer

Gross Wt. (Kg)	Tare Wt. (Kg)	Net Wt. (Kg)	Total Oil Collected (Kg)
4.52	1.60	2.92	2.92

4.52
1.60
2.92

Excess Aqueous Phase

Gross Wt. (Kg)	Tare Wt. (Kg)	Net Wt. (Kg)	Total Excess Aqueous Phase (Kg)
3.40	1.12	0.94	0.94

-1.34
2.06

2.06
-1.12

* additional 1.34 H2O used to rinse 0.1 out of tank (subtract from this)

- Concentrate the aqueous layer until 70.3Kg of effluent has been removed. The effluent is collected in a previously tared 55 gallon drum and saved until a mass balance is reconciled. Maintain the temperature at 45°C ± 2°C (113°F ± 4°F).

* Remember to take off 20 Kg H2O in system from heat-up

Total 90-91 Kg

Concentration Effluent

	Effluent #1	Effluent #2	Effluent #3	Effluent #4	Effluent #5	Effluent #6
Gross Wt. (Kg)	22.68	22.03	21.02	15.5		
Tare Wt. (Kg)	1.60	1.60	1.60	1.6		
Net Wt. (Kg)	21.08	20.43	19.42	13.9		
Total Effluent Collected (Kg)	21.08	41.54	60.96	74.86		

Effluent Collection Drum
Gross Wt. (Kg) _____
Tare Wt. (Kg) _____
Net Wt. (Kg) _____

Start Concentration 10:07 Finish Concentration 11:05

Process Temperature During Concentration

* heat measured @ outlet

Time	10:10	10:30	10:38	11:02	11:05				
Temp	52	42.5	43.0	45	45				

Date Processed: 12/1/98 **By:** [signature]

Process Temperature During Diafiltration

Time	11:05	11:25	11:40	11:52	12:08	12:25	12:37	12:57	12:16
Temp	45.0	42.0	42.0	43.0	43.5	44.0	44.0	42.0	43

Process Temperature During Diafiltration

Time	1:54	2:07	2:31						
Temp	46	46	47						

Diafiltration Start Time 11:05 Diafiltration Stop Time _____

- **PROCESS NOTE:** A diafiltration volume is defined as the final concentrated volume, in this case, ~~43.5~~ 55 Kg. → based on 2x conc for optimum flux rates

- When ultrafiltration is complete, sample the final product for duplicate Karl Fisher water analysis. Label the sample GNP_____. Maintain 45°C ± 2°C (113°F ± 4°F) while analysis is in progress.

Final Conc of additional Kg needed

- **PROCESS NOTE:** Expected KF value is approximately 77.5%.

Karl Fisher Analysis

KF Analysis #1 (%H2O)	KF Analysis #2 (%H2O)	Average KF (%H2O)

* Final conc product has milky appearance, cannot be further processed to capsules (residual oil?)

Date Processed: 12/1/98 **By:** Will Lott

- Based on the Karl Fisher water analysis, determine the quantities of virgin gelatin and glycerin required to proceed to a _____Kg gel mass production with _____% recycled gelatin and subsequent capsule manufacturing.

  Virgin Gelatin Requirement _____Kg

  Calculation:

- Determine a mass balance on the completed process.

  - Initial Netting Used _____Kg
  - Initial Water Charged _____Kg
  - Oil Phase Collected _____Kg
  - Excess Water From Oil Phase Collection _____Kg
  - Effluent From Concentration Step _____Kg
  - Water Charged For Diafiltration _____Kg
  - Effluent From Diafiltration _____Kg
  - Final Product(excluding system hold-up) _____Kg
  - Final Product(including system hold-up) _____Kg

- Calculations:
  - % Oil for Netting Used

  - Water In v. Effluent Out

  - Gelatin In v. Gelatin Out

- Perform ultrafiltration until 3 diafiltration volumes of deionized water have been achieved, in this process 3 diafiltration volumes is ~~130.5~~ 165Kg. The deionized water for diafiltration is preheated to 45°C ± 2°C (113°F ± 4°F).

11:05-53 to DV1

Deionized Water for Diafiltration DV2 DV3

	Charge #1	Charge #2	Charge #3	Charge #4	Charge #5	Charge #6
Gross Wt. (Kg)	55.0	55.0	55.0	55.0		
Tare Wt. (Kg)	0	0	0	0		
Net Wt. (Kg)	55.0	55.0	55.0	55.0		
Temperature (°C)	44	46	45.5	45		
Total Water Charged (Kg)	55.0	110.0	165.0	220		

Deionized Water for Diafiltration

	Charge #7	Charge #8	Charge #9	Charge #10	Charge #11	Charge #12
Gross Wt. (Kg)						
Tare Wt. (Kg)						
Net Wt. (Kg)						
Temperature						
Total Water Charged (Kg)						

45 min DV1 Finished @ 11:53

DV2 finished @ 1238

45 min

Diafiltration Effluent

	Effluent #1	Effluent #2	Effluent #3	Effluent #4	Effluent #5	Effluent #6
Gross Wt. (Kg)	21.50	20.62	15.82	20.70	20.18	21.10
Tare Wt. (Kg)	1.60	1.60	1.60	1.60	1.60	1.60
Net Wt. (Kg)	19.90	19.02	14.22	19.10	18.58	19.50
Total Effluent Collected (Kg)	19.90	38.92	53.14	72.24	90.82	110.32

DV3 12:37 - 145 Finish @ 1:45

DV4 = Finish @ 2:30

Diafiltration Effluent

	Effluent #7	Effluent #8	Effluent #9	Effluent #10	Effluent #11	Effluent #12
Gross Wt. (Kg)	22.48	22.74	15.84	20.90	20.64	12.54
Tare Wt. (Kg)	1.60	1.60	1.60	1.60	1.60	1.60
Net Wt. (Kg)	20.88	21.14	14.24	19.30	19.04	10.94
Total Effluent Collected (Kg)	131.20	152.34	166.58	175.88	194.92	205.86

+5

DV5 @ 6 N = 20.54

T = 1.6KG N Total

A.B.T., L.L.C.

Pilot Manufacturing Directions **Revision Date: 4/27/00**
Gelatin Recovery **Revision: 1**
Batch No: Intergel 050100-1

Procedure **Initial & Date**

3. When the water has reached 48°C ± 2°C (118°F ± 4°F), charge the gelatin netting for dissolution while maintaining mild mixing.

Waste Netting For Dissolution

	Charge #1	Charge #2	Charge #3
Gross Wt. (Kg)	47.05		
Tare Wt. (Kg)	5.45		
Net Wt. (Kg)	41.60		

Total Netting Charged 41.60 Kg

Temperature Before Netting Charge 42.0 °C/°F 42.3

Temperature After Netting Charge ____ °C/°F

Netting Charge Start Time 0850

Netting Charge Finish Time 0900

Mixer On yes

RPM —

Netting Type Used Vitamin E

Netting
Batch # 120741 WS 5/2/00
Formula 23
Product 500031-119228
[redacted] Vit E

increased temp setting @ 0820 WS

temp rising @ 0850, begin netting charge

PROCESS NOTE: High mixing may result in the formation of a fine emulsion which is of sufficiently small size that it is either difficult to break and will not allow for efficient separation of the oil phase and/or residual oil.

Date Processed: 5/2/00 **Signature:** [signature]

Procedure **Initial & Date**

2. Begin mild mixing and heat the water to 48°C ± 2°C (118°F ± 4°F). Maintain 48°C ± 2°C (118°F ± 4°F) throughout the manufacturing process.

Mixer Type air-driven, dual propeller Lightnin Mixer Model XJA-33

Mixer No. N/A

Mixer On yes

RPM —

Heating Start Time ~~0600~~ } held overnight in tank preset to 48°C

Heating Stop Time _____ }

Initial Temperature 80.0 °C/°F

Final Temperature 42.0 °C/°F

WA 5/2/00

PROCESS NOTE: It is important to maintain 48°C ± 2°C (118°F ± 4°F) through the manufacturing process. Temperatures above 50°C (122°F) will accelerate degradation of the gelatin.

Date Processed: 5/2/00 **Signature:** [signature]

Procedure **Initial & Date**

4. Allow the netting to mix (mild mixing) for 15-30 minutes until all the gelatin netting has dissolved. Use a plastic or stainless steel rod to check for complete dissolution of the gelatin netting. If dissolution is not complete, mix an additional 15 minutes with mild mixing. Repeat if necessary

9:06 - mixer spds up as netting dissolution proceeds - slowed mixer to avoid emulsion formation

Initial Temperature 38.7 °C/°F

Final Temperature 40.0 °C/°F

Mixing Start Time 0900

Mixing Stop Time 0925

RPM —

very little remaining in valve indentation on mixer blade

Dissolution Complete _____YES (proceed step #5) ✓ NO (continue mixing)

Initial Temperature 40.0 °C/°F

Final Temperature 42.0°C/°F

Mixing Start Time 0925

RPM —

Mixing Stop Time 0955

Dissolution Complete ✓ YES (proceed step #5) _____NO (continue mixing) WL 05/02/00

Date Processed: 5/2/00 **Signature:** [signature]

A.B.T., L.L.C.

Pilot Manufacturing Directions — **Revision Date: 4/27/00**
Gelatin Recovery — **Revision: 1**
Batch No: Intergel 050100 - 1

4a. 10:45 - temp = 44.5 begin skimmer operation for gross oil removal (begin 10:55)

Procedure — **Initial & Date** WL 5/2/00

12:20 ~~11:55~~ - finish skimming, temp = 49.5

4b. filter thru 80 mesh bag into tank #21 G = 318.15 Kg, T = 196.50 Kg, N = 121.65 Kg.

5. While dissolution of the gelatin netting is in progress, perform micro swabbing then preheat the filtration unit to 48°C ± 2°C (118°F ± 4°F) by circulating hot process water through the unit for 15 minutes. Determine the system hold-up volume during this preheating step.

4b. ↓
Oil removed
G = 2774.40 Kg
T = 288.50 Kg
N = 2485.90 Kg
↳ separates into 2 layers

Micro Swabs Taken _____

Number of Micro Swabs _____

Swab Locations _____

Initial Outlet Temperature _____°C/°F

Final Outlet Temperature _____°C/°F

Circulation Start Time _____

Circulation Stop Time _____

System Hold-Up Volume _____Kg

PROCESS NOTE: It is important to preheat the filtration unit to avoid potential congealing of the aqueous gelatin layer.

4c. filter thru 10μ cartridge filter, tank #15
Start - - - initial temp = 49.1
Stop =

331.75
G = ~~2774.40~~ 212.05 Kg
T = ~~288.50~~
N = ~~2485.90~~ 119.7 Kg feed to MF
↳ ~~separates into 2 layers~~

6. When dissolution of the gelatin netting is complete, stop mixing and allow the mixture to stand for 30 minutes for separation of the oils.

↳ skimmer used see top next p-6

Mixer Off _____

Hold Start _____

Hold Stop _____

Date Processed: 5/2/00 **Signature:** Will Ly

Procedure **Initial & Date**

Initial Temperature _____°C,/°F

Final Temperature _____°C/°F

7. Using a skimmer, previously cleaned and inspected, remove the separated, upper oil layer to a previously cleaned, tared, appropriately sized collection container, .

Skimming Start _____

Skimming Complete _____ done - see p. 5

Initial Temperature _____°C/°F

Final Temperature _____°C/°F

Oil Layer Collected Gross Wt. _____Kg

Tare Wt. _____Kg

Net Wt. _____Kg

8. Collect a 2 ounce **sample** from the dissolution & microfiltration feed tank for residual oil analysis.

Sample Collected Gross Wt. _____g

Tare Wt. _____g

Net Wt. _____g

Date Processed: 5/2/00 **Signature:**_____

Procedure **Initial & Date**

9. If appropriate, separate the oil layer collected in Step #7 and obtain weights of the aqueous and oil layers and **sample** of the aqueous layer for analysis and mass balance calculations.

   Oil Layer Collected Gross Wt. _____Kg

   Tare Wt. _____Kg

   Net Wt. _____Kg

   Aqueous Layer Collected Gross Wt. _____Kg

   Tare Wt. _____Kg

   Net Wt. _____Kg

10. Prepare a clean, tared, previously inspected, appropriately sized, stainless steel tank (microfiltration permeate & ultrafiltration feed/retentate tank) equipped with a heating jacket and variable speed mixer. Swab the tank for micro analysis then preheat the tank to 48°C ± 2°C (118°F ± 4°F).

    Micro Swabs Taken _____

    Number of Micro Swabs _____

    Swab Locations _____

    Tank Size _____

    Tank No. _____

    Tank Tare Wt. _____Kg

    Tank Temperature _____°C/°F

Date Processed:_____ **Signature:**_____

A.B.T., L.L.C.

Pilot Manufacturing Directions — **Revision Date: 4/27/00**
Gelatin Recovery — **Revision: 1**
Batch No: Intergel 050100-1

Procedure — **Initial & Date**

1. Charge deionized water for netting dissolution to a clean, tared, previously inspected and swabbed, appropriately sized, stainless steel tank (netting dissolution & microfiltration feed tank) equipped with a heating jacket variable speed mixer.

   Tank Size ≈40 gal

   Tank No. 3

   Tank Tare Wt. 201.65 Kg — WA 5/1/00

   Micro Swab Taken no

   Number of Swabs —

   Swab Locations —

Deionized Water For Waste Netting Dissolution

	Charge #1	Charge #2	Charge #3
Gross Wt. (Kg)	285.10		
Tare Wt. (Kg)	201.65		
Net Wt. (Kg)	83.45		

284.80 − 201.65 = 83.15

weight recheck 5/2/00 @ 7:30a.

Total Water Charged 83.45 Kg — WA 5/1/00

$2\overline{)183.15} = 41.57$

41.57 + 5.45 = 47.02

Date Processed: 5/1/00 **Signature:** Will Lee

Supporting Documentation For Paragraphs 12 & 15 Of The Attached Response & Inventor Declaration

The present application was successful at removing emulsified oils, by the use of tangential flow microfiltration, that was not possible or obvious from what was fairly disclosed by the '408 patent (the batch record is enclosed, 1 of 4 batches processed at this time).

Residual oil analysis resulted in no detectable oil after tangential flow microfiltration (analysis was done pre-microfiltration, but after cartridge pre-filtration (as used in the '408' patent) which showed presence of residual oils). Clear evidence that '408' could not remove hydrophilic, emulsified oily contaminants.

All post process testing showed the present application to be a complete success at recycling waste gelatin netting into new soft gelatin capsules.

Procedure **Initial & Date**

11. Turn on the preheated filtration unit and begin microfiltration to remove residual oil contamination. At the predetermined concentration of the feed solution, add one volume of process water and diafilter the feed solution to maximize gelatin & glycerin throughputCollect the microfiltration permeate in the tank described in Step #10.

Membrane Pore Size _____

Membrane Lot# _____

Membrane Surface Area _____

Process Flow Rate _____

Microfiltration Start Time 1307 @ ~~45~~ 44.6°C WA 5/2/00 initial gel. conc = 16%

Concentration at Diafiltration Start 1330 – 6 x 5 L in a 5 L bucket

Diafiltration Start Time 1330

Water for Diafiltration Gross 30 Kg

Tare 0 Kg

Net 30 Kg

Temp. ~37 °C/°F

Microfiltration Finish 1345

Flux Rates see attached

Transmembrane Pressures see attached

Process Temperature During Microfiltration (30 minute intervals)

Time	1307							
Temp. °C	~~45.0~~ 44.6 WA 5/2/00							

Date Processed: 5/2/00 **Signature:** [signature]

A.B.T., L.L.C.

Pilot Manufacturing Directions — **Revision Date: 4/27/00**
Gelatin Recovery — **Revision: 1**
Batch No: Integel 050100-1

Procedure — **Initial & Date**

12. Collect a 2 ounce **sample** from the microfiltration permeate & ultrafiltration feed/retentate tank for residual oil analysis.

    Sample Collected Gross Wt. _____ Kg

    Tare Wt. _____ Kg

    Net Wt. _____ Kg

13. Weigh the dissolution & microfiltration feed tank to determine the mass of unprocessed material. Collect a 2 ounce **sample** for water and glycerin analysis for mass balance calculations. Make the assumption that the material in the hold-up volume is of the same composition as this sample.

30 kg water in for diafiltrat

14. Weigh the microfiltration permeate and hold at 48°C ± 2°C (118°F ± 4°F) while cleaning the microfiltration system and membranes.

    Microfiltration Permeate Gross Wt. 314.65 Kg
    Tank #3

    Tare Wt. 201.65 Kg

    Net Wt. 113.00 Kg

    Hold Start 1345

    Initial Temp 43 °C/°F

    Hold Finish 1400

    Final Temp 43.4 °C/°F

Residual MF Feed G =

T =

149.7 − 113.0 → N = 36.7 kg

initial 119.7 kg in MF Feed
30 kg diaf. vol
149.7

Date Processed: 5/2/00 **Signature:** [signature]

Procedure **Initial & Dat**

15. Clean the microfiltration unit using the procedure described below. Monitor the cleanability of the membrane (see attached membrane cleaning/regeneration data). Swab the filtration unit for micro analysis.

    Micro Swabs Taken _____

    Number of Micro Swabs_____

    Swab Locations _____

    * flushed w/ hot water to remove gelatin -- cleaning to be done at end of UF cycle

Procedure **Initial & Date**

16. When the microfiltration unit and membrane cleaning is complete, install the ultrafiltration membranes for the concentration process, preheat the filtration unit to 48°C ± 2°C (118°F ± 4°F) by circulating hot process water through the unit for 15 minutes.

Initial Outlet Temperature _____°C/_°F

Final Outlet Temperature _____°C/°F

Circulation Start Time _____

Circulation Stop Time _____

N/A direct from MF to UF

PROCESS NOTE: It is important to preheat the filtration unit to avoid potential congealing of the aqueous gelatin layer being transferred.

17. Prepare a clean, tared, previously inspected, appropriately sized, stainless steel tank (ultrafiltration permeate tank) equipped with a heating jacket and variable speed mixer. Swab for micro analysis and preheat the tank to 48°C ± 2°C (118°F ± 4°F).

Tank Size _____

Tank No. 21

Tank Tare Wt. 196.50 Kg

Tank Temperature — °C/°F

250.40
196.50
53.90 Uf permeate

no heat needed

Date Processed: 5/2/00 **Signature:** [signature]

Procedure **Initial & Date**

18. Turn on the preheated filtration unit and begin ultrafiltration to concentrate the feed solution to the desired concentration of gelatin for recycle.

12

Membrane Pore Size _____

Membrane Lot# _____

Membrane Surface Area _____

Process Flow Rate _____

Concentration Start Time 1420

Concentration Finish Time 1510

Flux Rates see attached

Transmembrane Pressures see attached

* COA's for selatn + glycerin

Process Temperature (feed tank) During Concentration (30 minute intervals)

Time	1420	1430	1450					
Temp, °C	42.6	43.3	43.7					

19. When concentration is complete, weigh the microfiltration permeate & ultrafiltration retentate tank. Maintain 45°C ± 2°C (113°F ± 4°F) while analysis is in progress.

Tank Gross Wt. ~~255.10~~ Kg

Tare Wt. 201.65 Kg

Net Wt. 53.45 Kg

6.6 l system holdup
53.9 l permeate
53.45
113.5

* some UF retentate lost to feed tank as Julia accidentally moved the recirc hose to retentate tank

Date Processed: _____ **Signature:** _____

* clear amber appearance

Procedure **Initial & Date**

20. When concentration is complete, obtain a 4 ounce **sample** from the feed tank for duplicate water analysis by LOD and duplicate glycerin analysis by GPHPLC. Maintain 45°C ± 2°C (113°F ± 4°F) while analysis is in progress.

Water & Glycerin Analysis

LOD (%H2O)	GPHPLC (Glycerin)
Analysis #1	Analysis #1
Analysis #1	Analysis #2
Average LOD	Average

21. Weigh the ultrafiltration permeate tank to determine the mass of permeate removed. Obtain a 2 ounce **sample** for water & glycerin analysis for mass balance determination.

Permeate Tank Gross Wt._____Kg

Tare Wt. _____Kg

Net Wt. _____Kg

Sample Collected Gross Wt. _____g

Tare Wt. _____g

Net Wt. _____g

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

22. Based on the analysis in Step #19, determine the quantities of virgin gelatin and glycerin required to proceed to gel mass production with _____% recycled gelatin and subsequent capsule manufacturing.

Virgin Gelatin Requirement _____

Virgin Glycerin Requirement _____

Calculation: Glycerin from previous gel mass – COA water content _____

Lot No. _____

Gelatin from previous gel mass -- COA water content _____

Lot No. _____

Procedure **Initial & Date**

Calculation:

a. Glycerin Assay (average from Step #20) / COA Assay = Actual Glycerin Content in Final Concentrated Gel Mass

b. Gelatin Content in Final Concentrated Gel Mass = (100% - (Glycerin Assay = Water Assay)) / (100% - Gelatin COA Water Content)

c. Water Content in Final Concentrated Gel Mass = 100% - (a. and b. above)

Procedure **Initial & Date**

23. Determine a mass balance on the completed process.
    - Water

    a. Water input
        i. System hold-up _____
        ii. From netting input _____
        iii. Initial dissolution volume _____
        iv. Microfiltration diafiltration volume _____
            1. Total water input _____

    b. Water out
        i. Residual from microfiltration feed tank _____
        ii. Excess from oil skimmer operation _____
        iii. Concentration permeate _____
        iv. In final concentrated retentate _____
            1. Total water accounted for _____

    c. Water mass balance (water out / water input) _____

Procedure **Initial & Date**

- Gelatin

a. Gelatin input
   1. From netting input _____

b. Gelatin out
   1. Residual from microfiltration feed tank _____
   2. From oil skimmer operation _____
   3. Concentration permeate _____
   4. In final concentrated retentate _____

c. Total gelatin accounted for _____

d. Gelatin mass balance (gelatin out / gelatin input) _____

- Glycerin input

a. From netting input _____

b. Glycerin out
   1. Residual from microfiltration feed tank _____
   2. From oil skimmer operation _____
   3. Concentration permeate _____
   4. In final concentrated retentate _____

ii. Total glycerin accounted for _____

- Glycerin mass balance (glycerin out / Glycerin input) _____

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

24. Samples Points for Analysis

- Step 8 Microfiltration feed tank after skimming Residual Oils

  1. Result _____

- Step 9 Aqueous portion of skimmed layer Water /Glycerin/Gelatin

  1. Results Water _____

     Glycerin _____

     Gelatin _____

- Step 12 Microfiltration final permeate Residual Oils

  1. Result _____

- Step 13 Microfiltration residual feed Water /Glycerin/Gelatin
  1. assume system hold-up has same composition

  2. Results Water _____

     Glycerin _____

     Gelatin _____

Procedure

Initial & Dat

- Step 20 Final concentrated gel mass Water /Glycerin/Gelatin

  1. Results Water _____

     Glycerin _____

     Gelatin _____

- Step 21 Ultrafiltration permeate Water /Glycerin/Gelatin

  1. Results Water _____

     Glycerin _____

     Gelatin _____

- Micro Analysis
  a. Step 1
     1. dissolution tank _____
     (prior to water charge for dissolution of netting)

  b. Step 5
     1. filtration unit _____
     (prior to system preheating & microfiltration)

  c. Step 10
     1. microfiltration permeate _____
     (prior to start of microfiltration permeate collection)

  d. Step 15
     1. filtration unit _____
     (after post microfiltration cleaning)

  e. Step 26
     1. filtration system _____
     (post ultrafiltration cleaning – to be stored)

Date Processed:_____ **Signature:**_____

Procedure

Initial & Dat

25. Attachments
    - Flux Profiles
    - Pressure profiles
    - Membrane cleaning/regeneration profiles
    - QC analysis sheets

26. Clean the filtration unit using the procedure described below. Monitor the cleanability of the membrane (see attached membrane cleaning/regeneration data). Swab the filtration unit for micro analysis.

    Micro Swabs Taken _____

    Number of Micro Swabs_____

    Swab Locations _____

215-657-

48°C = 118°F

May 1, 200

Bob Mack availability ⇒ 1:30 → 4:30
↳ 609-951-6604 for

phone ⇒ 609-951-6602 Ref: ① Mill pave conte

Bob c home after 7pm ② Financing
732-536-3246

①

Tank (preset to 48°C)

#3	116°C	Tare = 201.65 ~~199.65~~ Kg
#15	116.2°C	Tare = 212.05 Kg
#21	120.3°C	Tare 196.50 Kg

Diss Tank
285.10
~~201.65~~
83.45 Kg

sol conc = ~~22.83~~ 22.8%

6.58 glycerin
25% recycle = 14.26 gelatin
41.62 ~~43.30~~ water
~~1.11~~ 67.46

May 2, 2000

* 125 Kg gel mass (experimental for Ross Tank Operation)
gelatin (45.64) = 57.05 Kg gelatin
glycerin (21.06) = 26.33 Kg glycerin
water (34.64) = 43.3
101.34% 43% water initially
126.68 Kg

viscosity after melter 8-20K (12-13 avg for Delft gelatin

May 2, 2000

53.45 kg process material
↳ 73% H_2O
5.1% glycerol

glycerol $\frac{2.72 \text{ kg}}{.98}$ glycerol = 2.78 kg

water 39.02 = 37.73

41.8

gelatin 11.65 / .9 = 12.94 kg

5345

37.73 kg H_2O ÷ .3464 = 108.9 kg

↳ 25% gelatin = 12.42 kg

May 2, 2000

INTERGEL: Division of IMC Industries, Inc. BATS #120854

RAW MATERIAL IDENTIFICATION CARD

Product Description: N/A

Product Lot No.: N/A

Raw Material Description: GLYCERINE

Raw Material Code: 300263

Raw Material Lot No.: 118520

Net Weight: 21.05 KG

Weighed By: [signature]

Date: 5/2/00

GELATIN BATCH # 120854

Glycerine

11:25AM 05-02-00
ID - 00
24.50 kg GR
3.45 kg TR
21.05 kg NT

LOT # 118520

INTERGEL: Division of IMC Industries, Inc.

RAW MATERIAL IDENTIFICATION CARD

Product Description: N/A

Product Lot No.: N/A

Raw Material Description: GELATIN D 150

Raw Material Code: 300260

Raw Material Lot No.: 117511

Net Weight: 45.65 KG

Weighed By: [signature]

Date: 5/2/00

11:44AM 05-02-00
ID - 00
51.30 kg GR
5.65 kg TR
45.65 kg NT

May 2, 2006

54.45 Kg recovered / c gel mass

glycerin	5.04%	21.06%
water	73.3%	34.64
gelatin		45.64

Glycerol 54.45 × 0.0504 ÷ .98 = 2.80 kg

water ~~39.91 kg~~ 54.45 − 2.8 − 13.04 = 38.56 kg

gelatin 54.45 − 2.80 − 39.91 ÷ .9 = 13.04 kg

38.56 kg ÷ .3464 = 111.32 kg gel mass

6:30pm 20.65 charged

Charges

glycerol 111.32 × .2106 − 2.80 = 20.64 kg

23.44 11.95% gly recycle

gelatin 111.32 × .4564 − 13.04 = 37.77 kg

50.81 25.7% gelatin recycle

6:40 Recor. mass + glycerol heating @ 20 rpm
80°C water feed to jacket

May 7, 2020

7:30 156.6°C — weigh gelatin

7:40 gel in, top down + mixing @ 2RPM

7:45pm partial vac applied, some foaming

Transfer tank G= 319.40

T= 211.45 kg

N= 107.95

8:15 vac applied & degassing evident

9:15 done, opened vessel, gel mass looks great

9:30 transfer thru "stocking" as per normal practice to tank #13

viscosity 10RPM 59.1°C

504

yield

107.95

111.32

96.97%

10:15 on heat as normal

Gel Mass Quality

Residual Oils Analysis

Evaporative Light Scattering Detection (ELSD) has become a popular analytical technique for evaluation of non-chromophoric entities, such as mineral oil, where UV detection is not an option. The ELSD detects mineral oil with good sensitivity in a time efficient manner.

Following is:

- Millipore Corporation Analyses
  - Post-microfiltration analyses
  - Subsequent gel mass analyses

- Alltech Associates Report Including:
  - Mineral oil & vitamin E standard curves
  - Low level mineral oil & vitamin E standard chromatograms
  - Pre & post-microfiltration analysis for mineral oil & vitamin E

Gel Mass Quality

Residual Oils Analysis

The following analyses were performed by Millipore Corporation using HPLC with ELSD. Alltech Associates developed the preliminary method of analysis and Millipore's analytical staff resolved some technical problems with reference to sample preparation. All samples were analyzed in triplicate. Millipore's ELSD method follows this results page.

SAMPLE ID	REPLICATE #	RESIDUAL OIL CONC., PPM
Hexane Blank	1	<20
	2	<20
	3	<20
Post MF/Recycle #1	1	<20
	2	<20
	3	<20
Post MF/Recycle #2	1	<20
	2	<20
	3	<20
Post MF/Recycle #3	1	<20
	2	<20
	3	<20
Post MF/Recycle #4	1	<20
	2	<20
	3	<20
Virgin Gel Mass	1	<20
	2	<20
	3	<20
Recycled Gel Mass #1	1	<20
	2	<20
	3	<20
Recycled Gel Mass #2	1	<20
	2	<20
	3	<20
Recycled Gel Mass #3	1	<20
	2	<20
	3	<20
Recycled Gel Mass #4	1	<20
	2	<20
	3	<20

Alltech Associates, Inc.
2051 Waukegan Road • Deerfield, IL 60015-1899
Phone: 847-948-8600 • Fax: 847-948-1078

October 12, 1999

William Schmidt
A.B. Technologies, L.L.C.
852 Redgate Road
Dresher, PA 19025-1431

Dear Dr. Schmidt,

Thank you for your interest in the Alltech Model 500 ELSD. We appreciate the opportunity to demonstrate how this powerful detector can aid in the analysis of mineral oil and vitamin E.

An isocratic, normal phase method was developed for the analysis of mineral oil and vitamin E. Both components gave a good response and eluted within ten minutes. Using the low-level standard chromatograms, the detection limits for mineral oil and vitamin E were calculated to be 10µg/mL and 0.5µg/mL respectively. Standard chromatograms and calibration curves are enclosed.

A preliminary sample preparation procedure was also developed to extract mineral oil and vitamin E from the sample matrix. Approximately 1g of each sample was weighed out, prepared and analyzed for mineral oil and vitamin E. In the preparation procedure, each sample was diluted 20x. We did not have the means or time to determine the percent recovery of the preparation procedure. Individual chromatograms and results of each sample are enclosed.

The Model 500 ELSD is ideal for analyzing samples with little or no UV chromophores. Because the ELSD's response does not depend on optical characteristics, it enables you to detect any non-volatile component in your sample. Since mineral oil is non-chromophoric, UV detection is not a viable option. The ELSD easily detects both components with good sensitivity in a timely manner.

Alltech is committed to providing you with a winning combination of products, equipment excellence and unrivaled technical support services. If you have any further questions regarding this analysis, please contact me or Melissa Wilcox at 800-255-8324.

Sincerely,

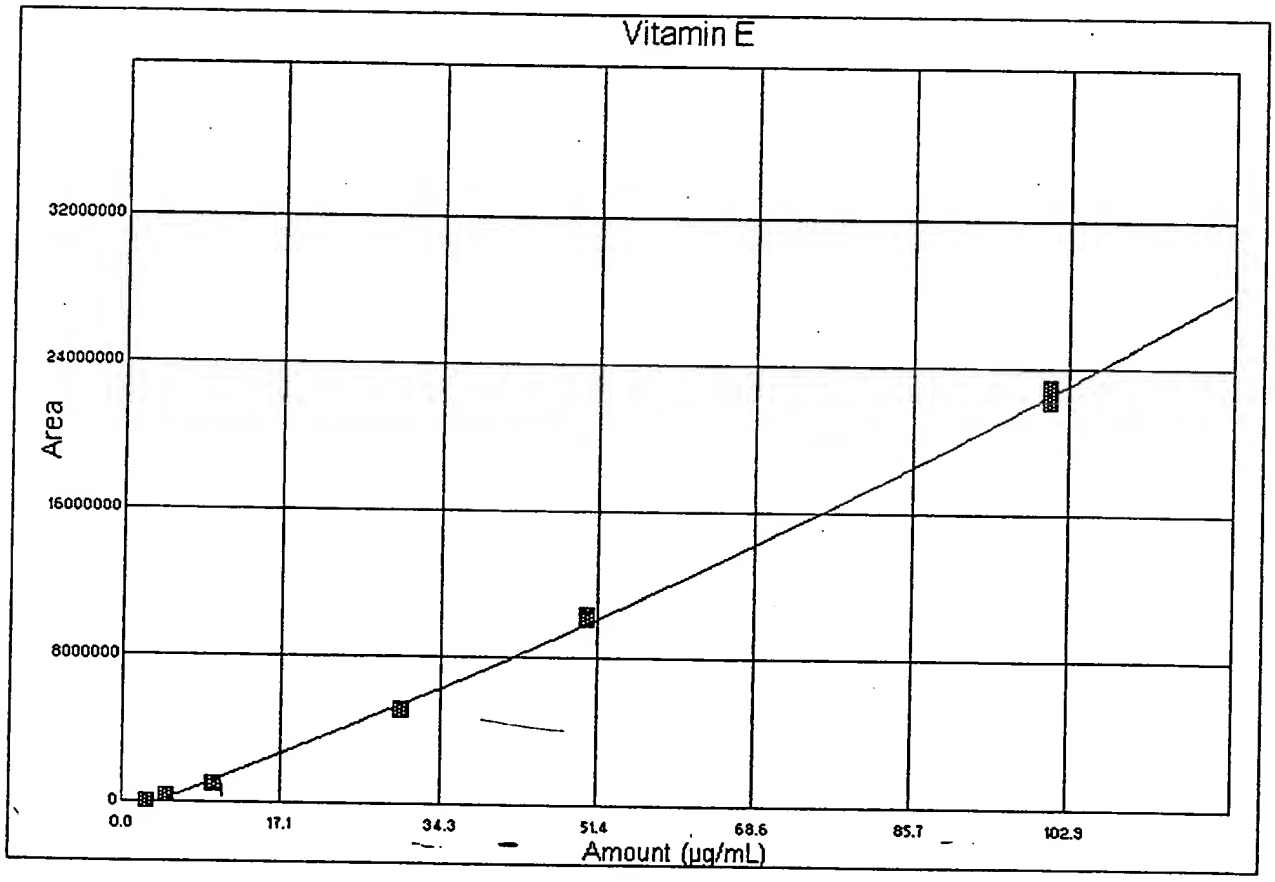
Michelle Chudy

Michelle Chudy,
Applications Chemist

cc: T. Jacobs, N. Olson, D. Lee, M. Wilcox

Alltech Associates, Inc.
2051 Waukegan Road • Deerfield, IL 60015-1899
Phone: 847-948-8600 • Fax: 847-948-1078

A.B. Technologies, L.L.C.
Vitamin E Standard Curve



Second Order Curve: $R^2 = 0.999$
Concentration Range: 3µg/mL - 100µg/mL

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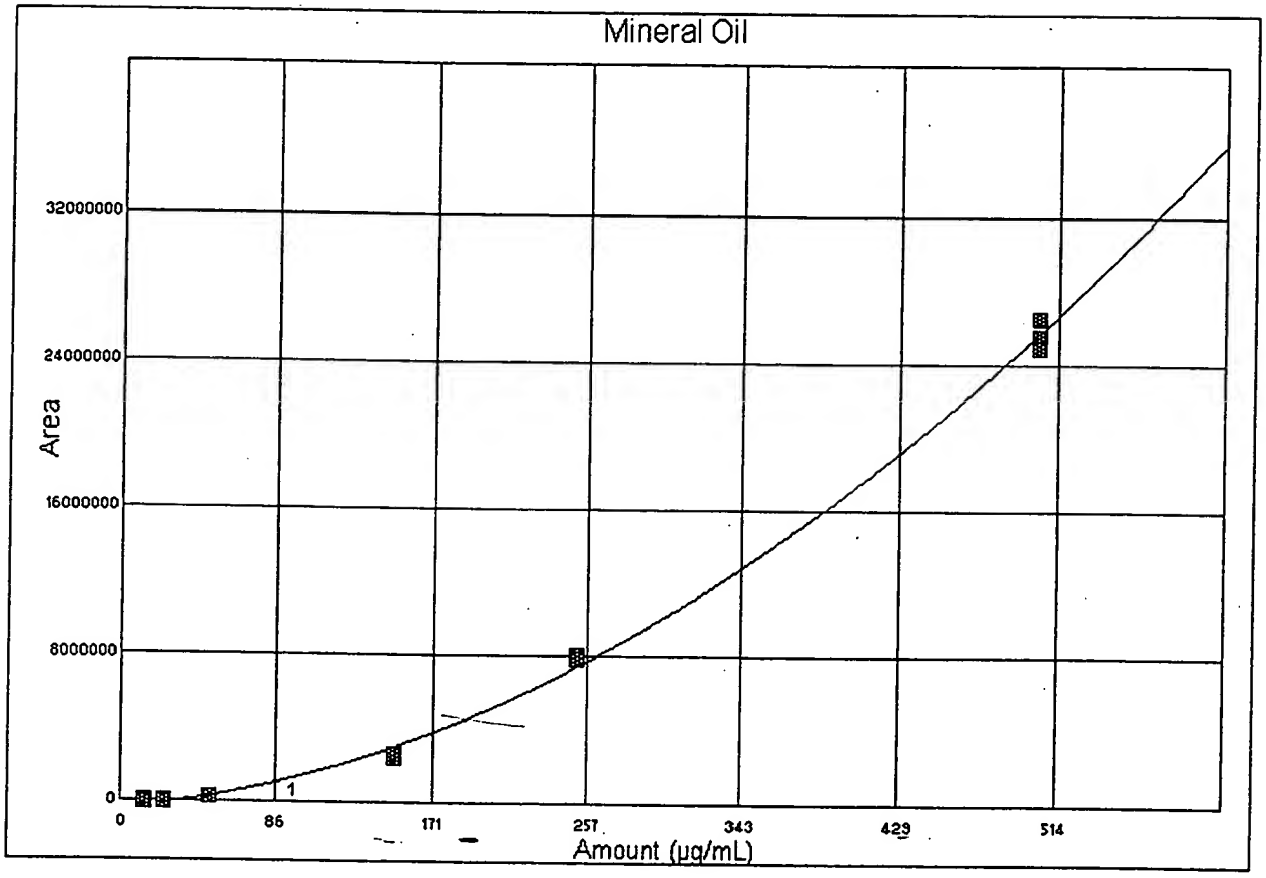
Phone: 847-948-8600 • Fax: 847-948-1078

A.B. Technologies, L.L.C.
Mineral Oil Standard Curve



Second Order Curve: $R^2 = 0.998$
Concentration Range: 15µg/mL - 500µg/mL

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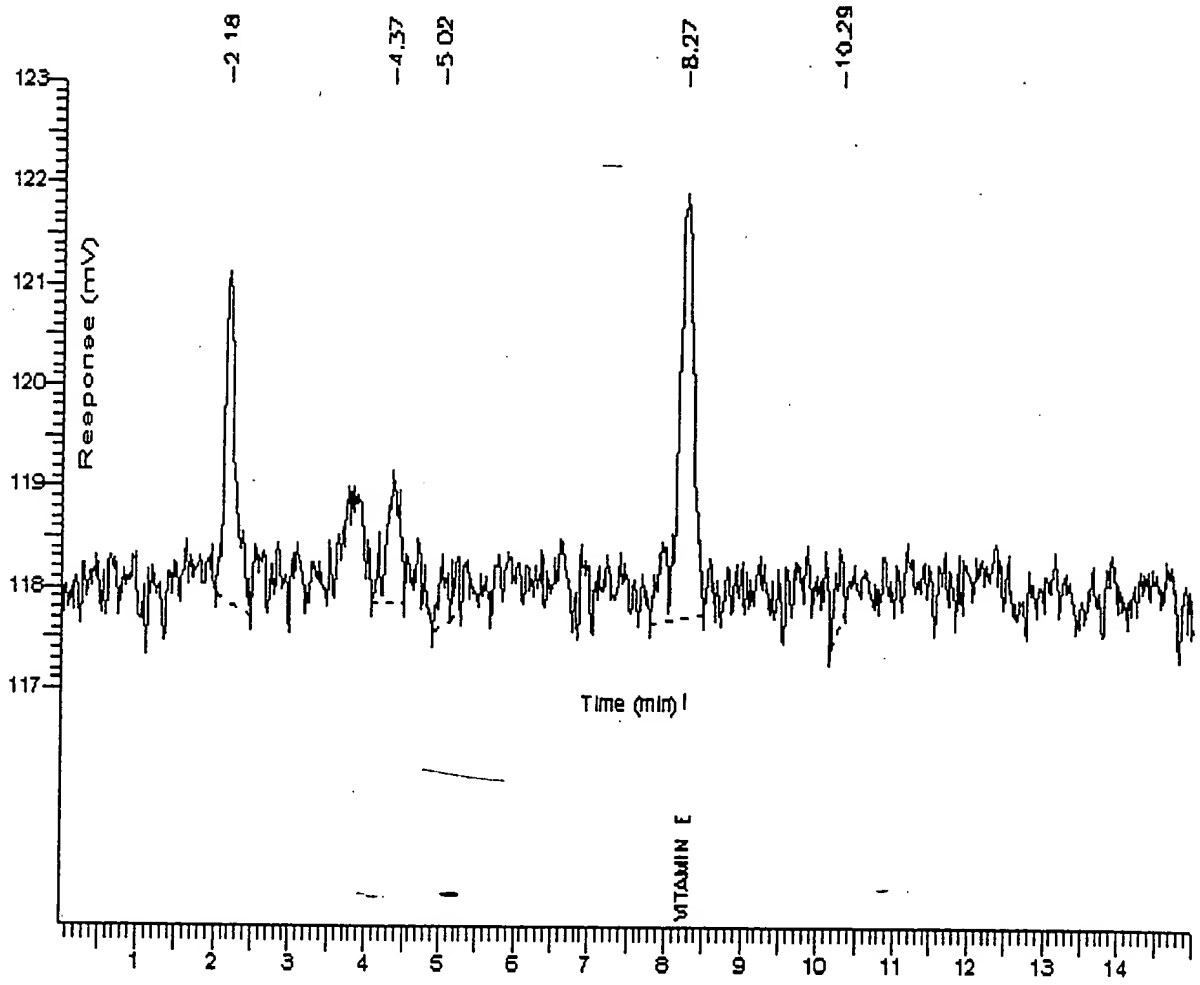
Phone: 847-948-8600 • Fax: 847-948-1078

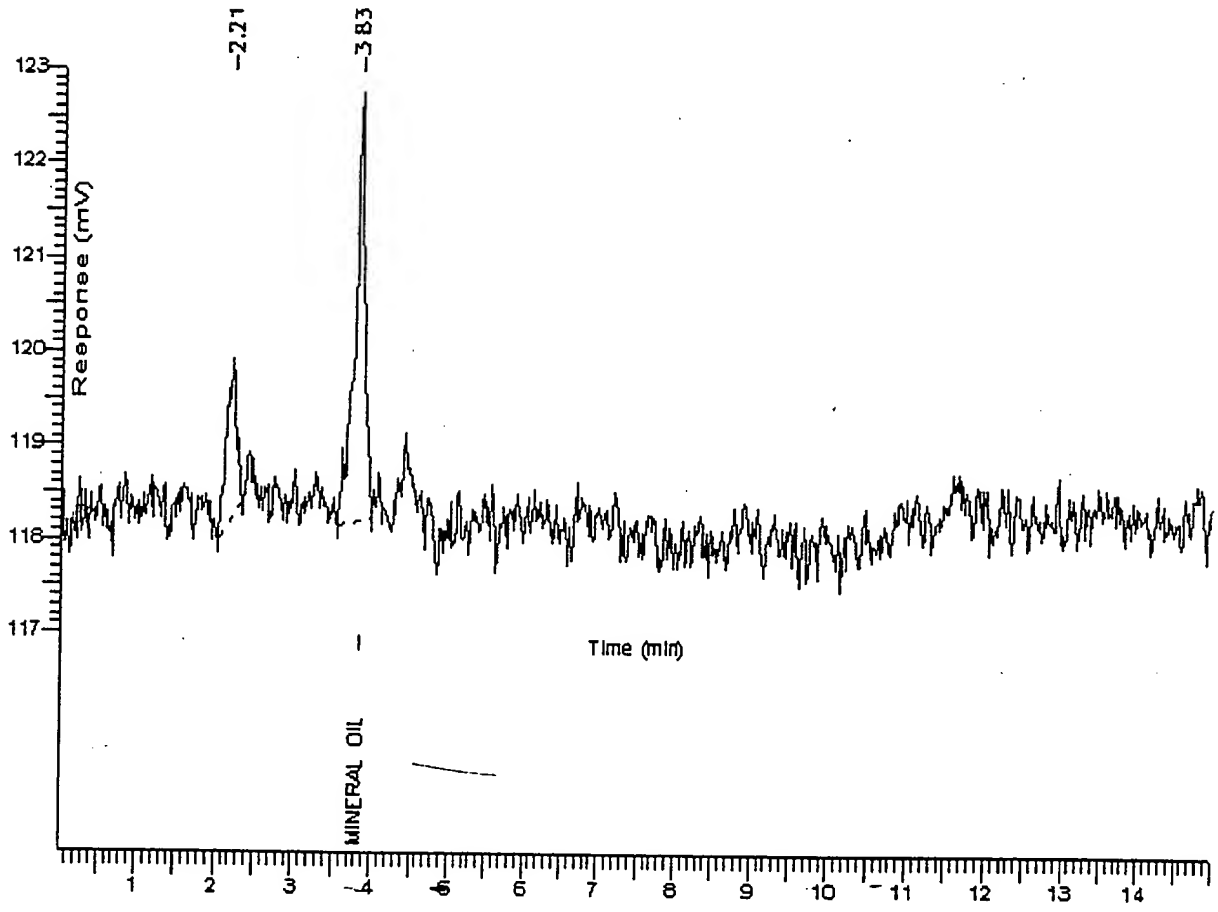
A.B. Technologies, L.L.C.
Low Level Vitamin E Standard



Concentration: 1µg/mL
Injection Volume: 20µL
Detector: Alltech 500 ELSD

Alltech Associates, Inc.
2051 Waukegan Road • De rfield, IL 60015-1899
Phone: 847-948-8600 • Fax: 847-948-1078

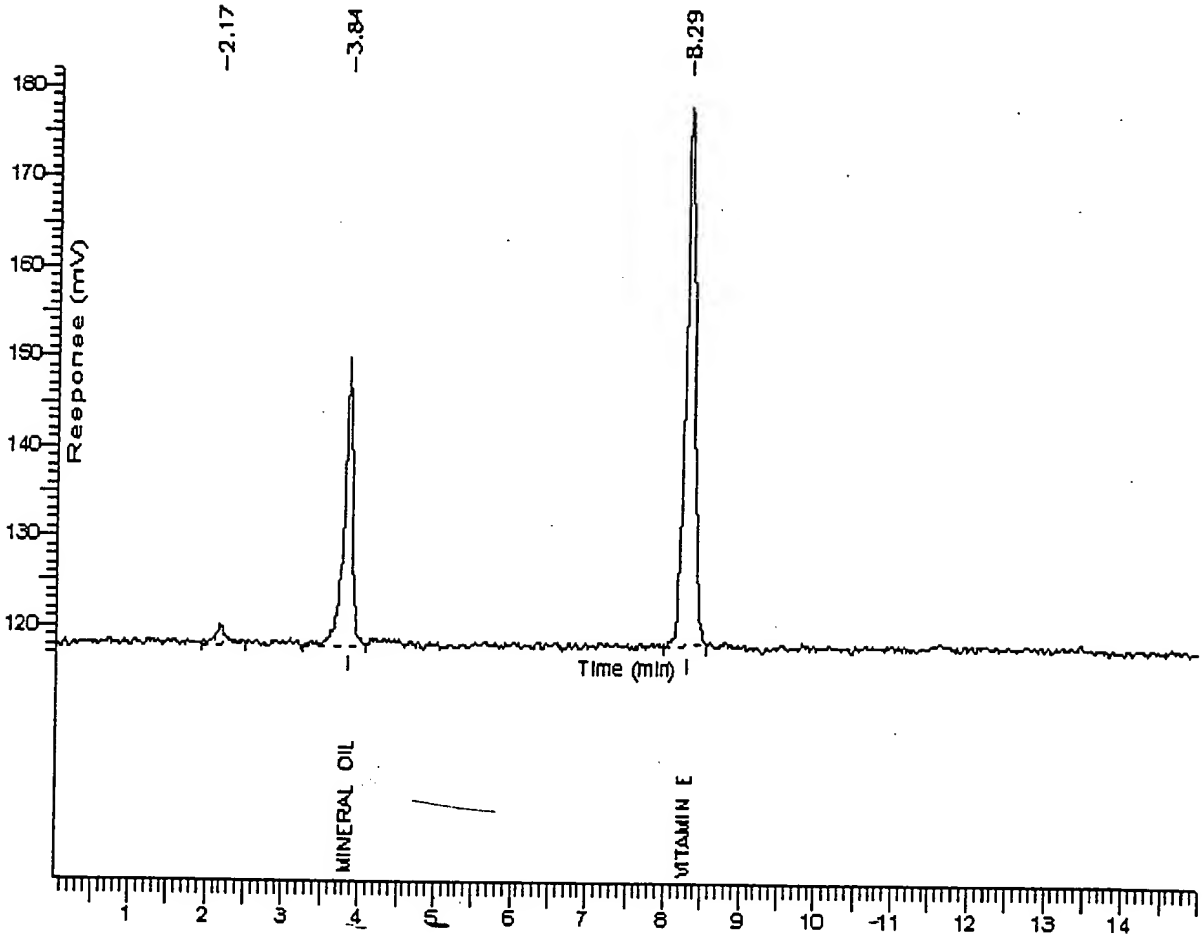
A.B. Technologies, L.L.C.
Low Level Mineral Oil Standard



Concentration: 15µg/mL
Injection Volume: 20µL
Detector: Alltech 500 ELSD

Alltech Associates, Inc.
2051 Waukegan Road • Deerfield, IL 60015-1899
Phone: 847-948-8600 • Fax: 847-948-1078

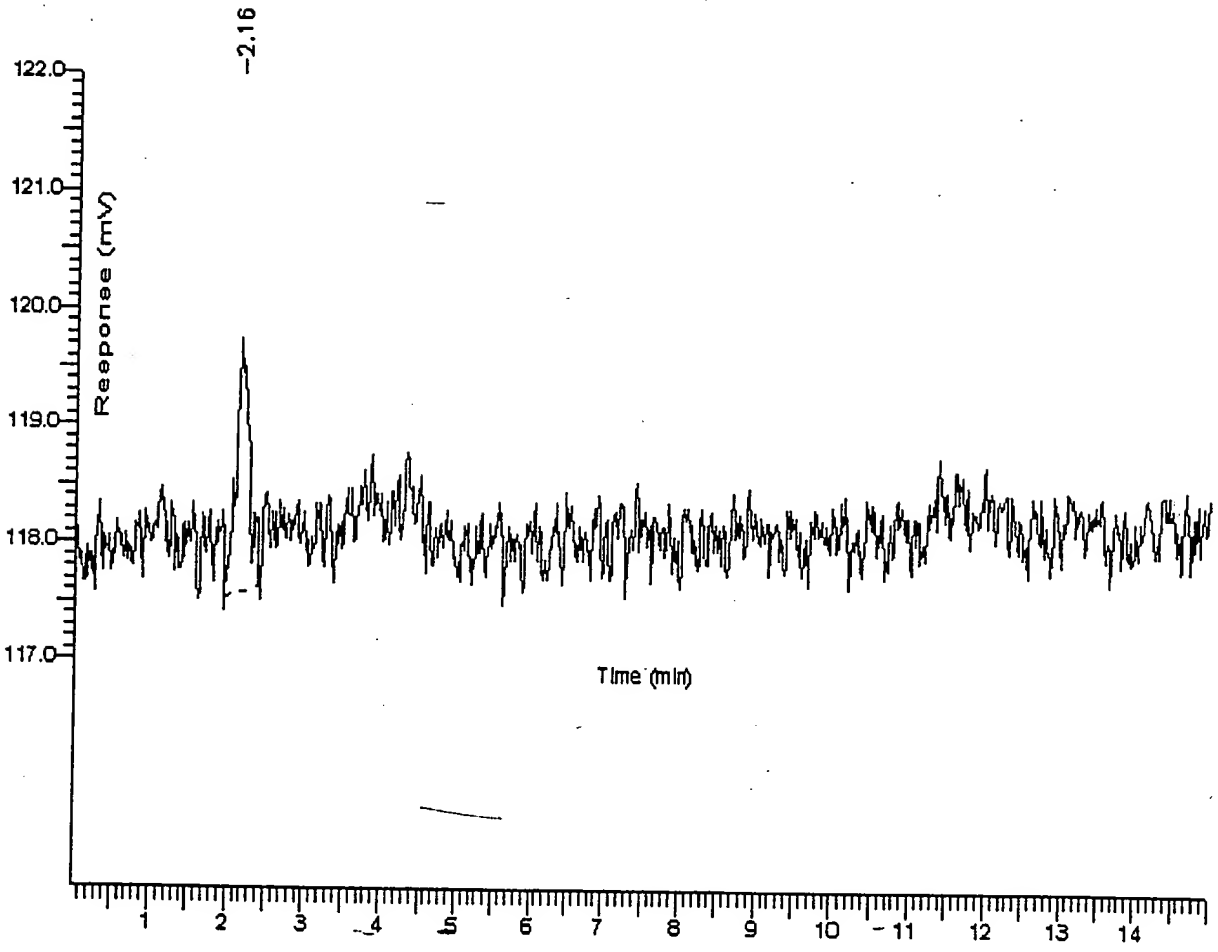
A.B. Technologies, L.L.C.
Pre-MF (20x Dilution)



Sample Amount: 1.06g
Calculated Concentrations:
Mineral Oil ~ 774µg/mL
Vitamin E ~ 119µg/mL
Injection Volume: 20µL
Detector: Alltech 500 ELSD

Alltech Associates, Inc.
2051 Waukegan Road • Deerfield, IL 60015-1899
Phone: 847-948-8600 • Fax: 847-948-1078

A.B. Technologies, L.L.C.
Post-MF (20x Dilution)



Sample Amount: 1.01g
Calculated Concentrations:
Mineral Oil ~ Not Detected
Vitamin E ~ Not Detected
Injection Volume: 20µL
Detector: Alltech 500 ELSD

Gel Mass Quality

Molecular Weight Distribution

The following data represents the molecular weight distribution analysis of gel masses prepared using between 25% to 30% recycled gelatin compared to a virgin gel mass. A comparison was also made to a gel mass after "current" recovery efforts, e.g., melt the netting at approximately 140°F for approximately 24 hours.

As illustrated here, ABT's recovery process is non-invasive to the gelatin integrity. The molecular weight distribution remains essentially unchanged in a gel mass manufactured using 30% recycled gelatin when compared to a virgin gel mass.

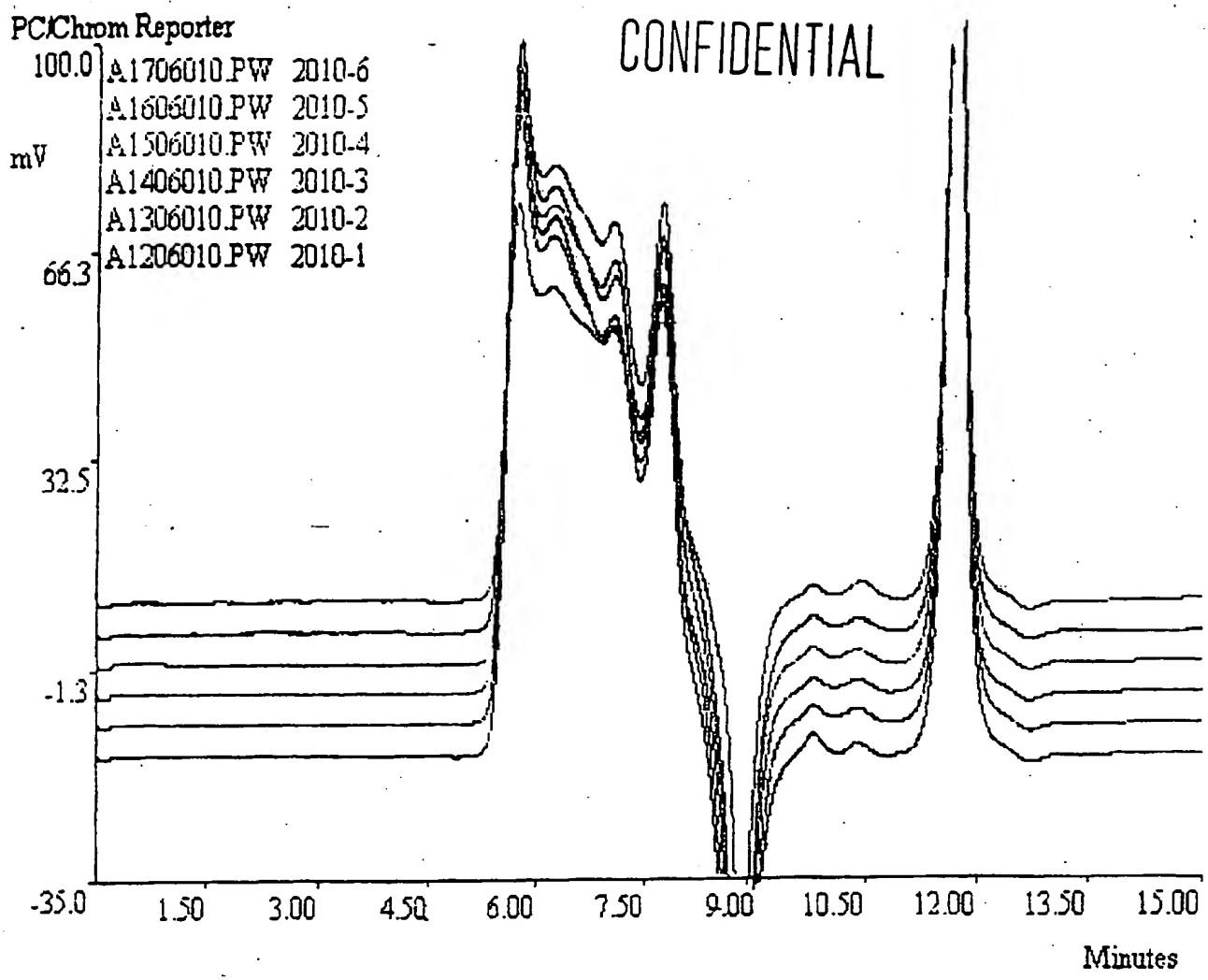
The tests were performed by Metrics, Inc. of Greenville, NC using the following chromatographic conditions:

- Instrument: A suitable HPLC equipped with a 100µl loop
- Column: Phenomonex Biosep SEC-S4000, 300x7.8mm , 5µm
- Column Temp: 40°C
- Mobile Phase: 0.5% sodium dodecyl sulfate
- Flow rate: 1.0 ml per minute
- Detection: Refractive Index
- Detector Temp: 50°C
- Standards: Pullulan standards from 853kDa to 5.8kDa

Key to Attachments

2010-1 = virgin gel mass (3119218)
2010-2 = recycled gel mass #1 (RD 050100-1)
2010-3 = recycled gel mass #2 (RD 050400-2)
2010-4 = recycled gel mass #3 (top sample) (RD 050800-3)
2010-5 = recycled gel mass #3 (bottom sample)
2010-6 = recycled gel mass #4 (RD 051000-4)
2010-7 = customer reclaimed gel mass

- RD 050100-1 was encapsulated using gelatin that was reclaimed from the netting from Intergel production batch #3119218 of Vitamin E 400IU capsules (100% virgin gel mass)
- RD 050400-2 was encapsulated using gelatin that was reclaimed from RD 050100-1 netting
- RD 050800-3 was encapsulated using gelatin that was reclaimed from RD 050400-2 netting
- RD 051000-4 was encapsulated using gelatin that was reclaimed from RD 050800-3 netting



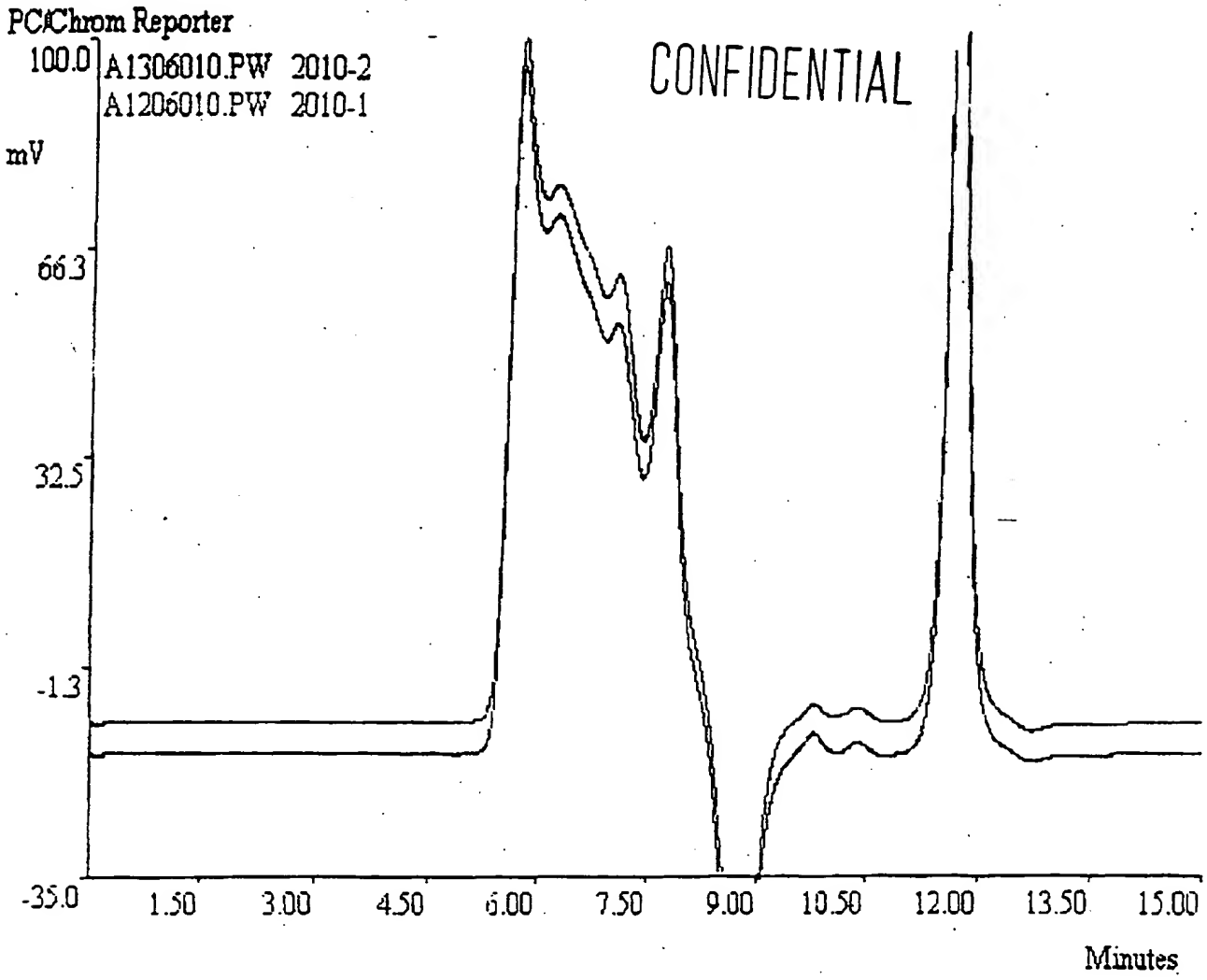
QUALITY ASSURANCE

mjt 6Jun00

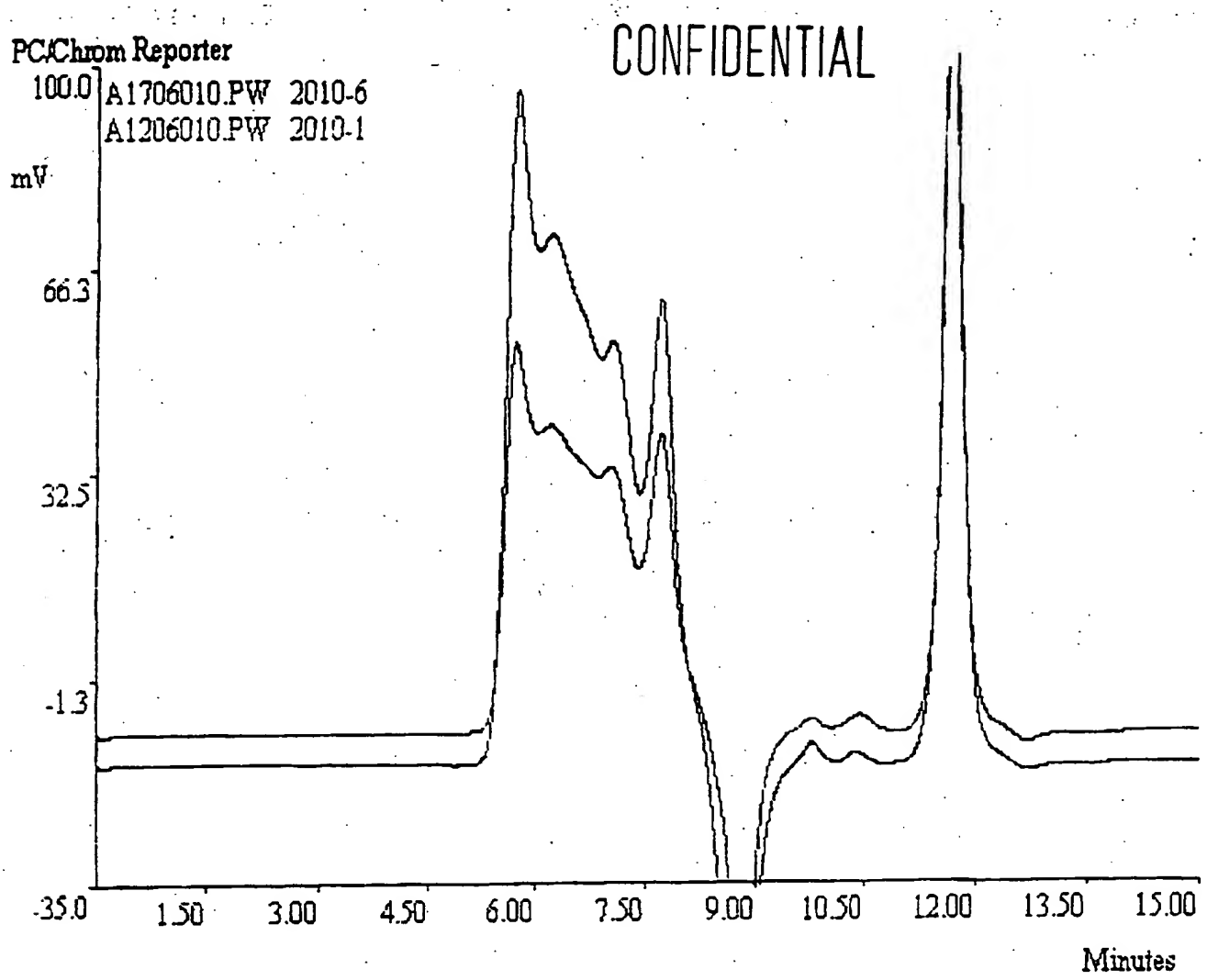
Approved by / Date

(16 chromatographic overlays)

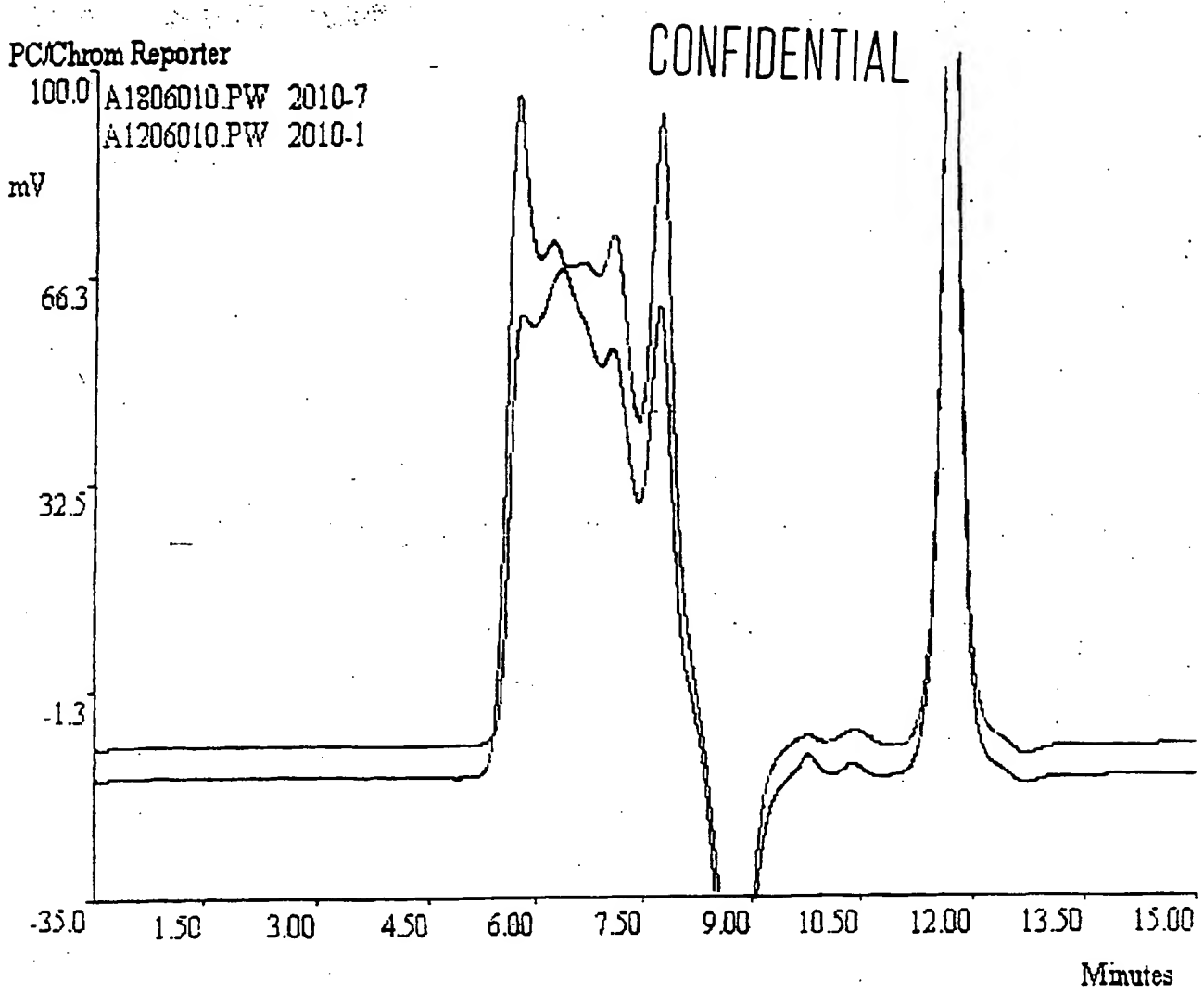
Overlay of the virgin gel mass and four consecutively recycled gel masses from ABT's gelatin recovery technology.



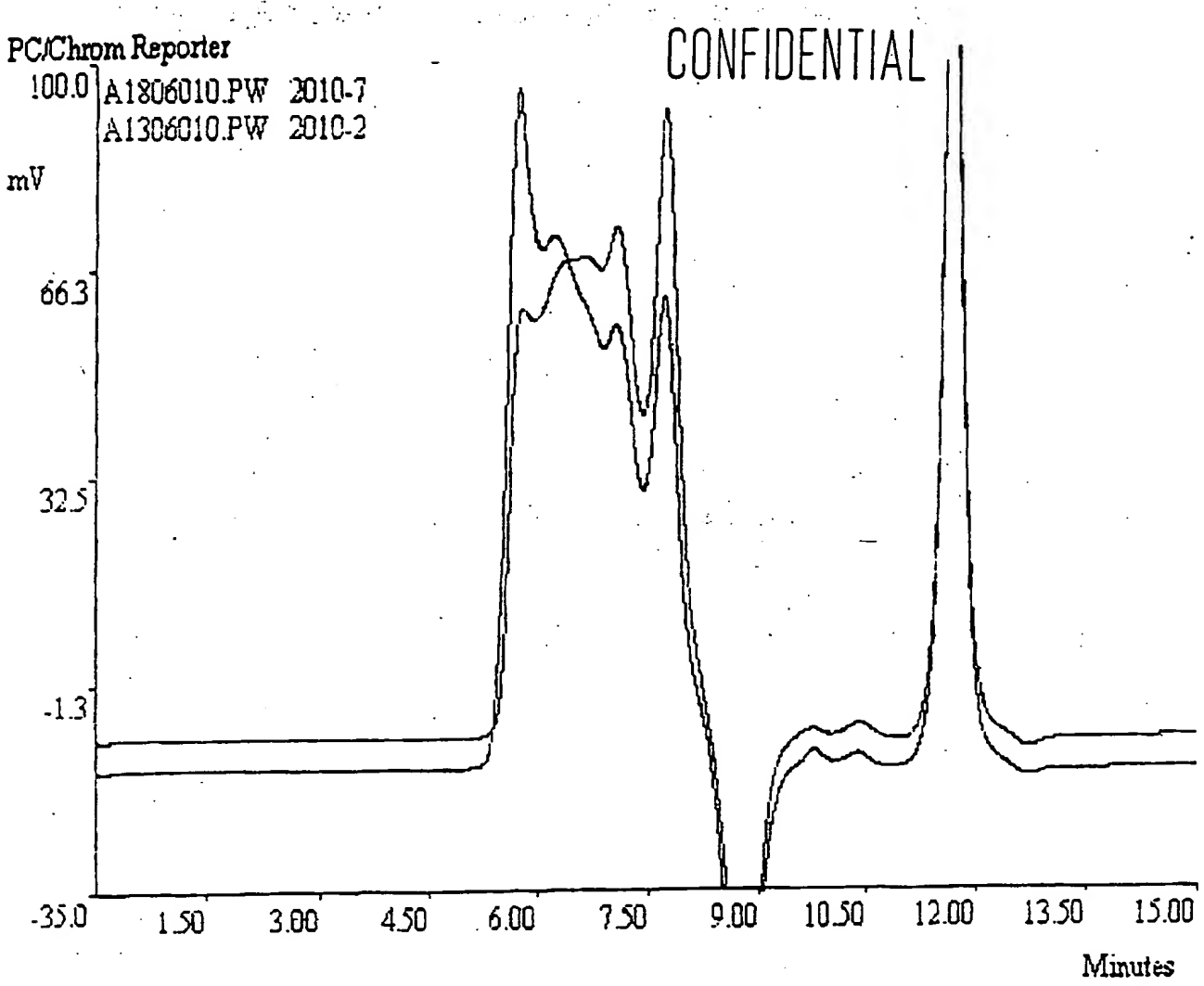
Overlay of virgin gel mass and ABT's first recycled gel mass



Overlay of virgin gel mass and ABT's fourth recycled gel mass. You will notice a smaller surface area for ABT's sample. This is due to less sample used for analysis. The peak shape and relative molecular weight distribution remain unchanged compared to the virgin gel mass.



Overlay of virgin gel mass and gel mass from the customer's current recovery operation. The virgin gel mass is represented by the large peak to the left of the overlay which is the higher molecular weight area of the chromatogram. This overlay clearly shows degradation of the gelatin, using "current" recovery techniques, and a shift to lower molecular weight fractions.



Overlay of ABT's first recycled gel mass and gel mass from the customer's current recovery operation. Again, the difference is clearly illustrated. The ABT recovery technology leaves the gel mass essentially unchanged. To the contrary, "current" recovery techniques degrade the gelatin dramatically. Overlaying any of the four ABT recycled gel masses with the gel mass resulting from "current recovery techniques will produce the same result.

Capsule Quality

The following data is derived from analysis of capsules manufactured from continuous recycle of gelatin and glycerin using ABT's recovery technology. As discussed below all capsules compare favorably to a control using zero recycled gelatin and glycerin.

Samples were analyzed for Rupture Strength (a measure of seal strength), Puncture Strength (a measure of capsule strength) and Adhesiveness:

- Seal strength of capsules manufactured from recycled gelatin and glycerin was equivalent to or better than the control capsule.
- Capsule strength of capsules manufactured from recycled gelatin and glycerin was better than the control capsules in all cases.
- No adhesive characteristic was found for the capsules manufactured from recycled gelatin and glycerin showing them to be equivalent or better than the control capsules
- In the results listed below, 'Force to Rupture' and 'Force to Puncture' are the measure of seal and capsule strength respectively. 'Gradient' and 'Distance to Rupture/Puncture' are a measure of the capsule's flexibility.

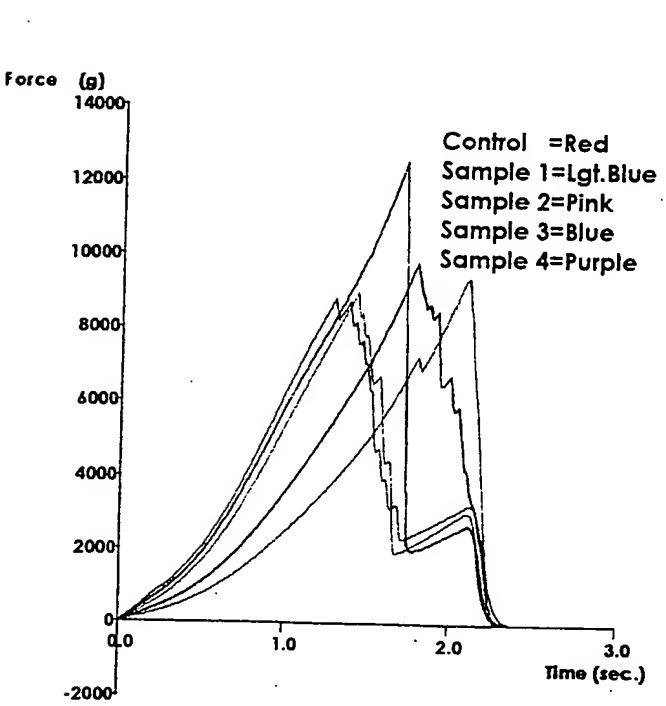
The tests were performed by Texture Technologies Corp. of Scarsdale, NY using their texture analyzer and the data below is from their report to ABT of June 28, 2000. A Rupture test was performed with the TA.XT2HRi Texture Analyzer, using a 50-kilogram load cell and Texture Expert Exceed Software. Adhesive and puncture test was also conducted using this instrument and a 5-kilogram load cell.

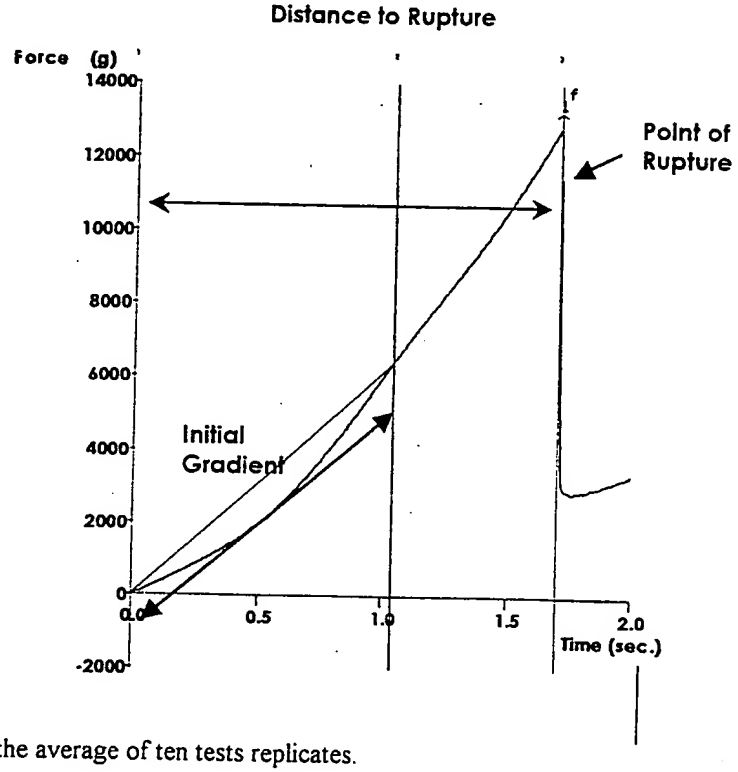
The test consisted of five samples provided by the A.B.T., L.L.C., Dresher, PA; 1) control lot # 119228, 2) RD 050100-1, 3) RD 050400-2, 4) RD 050800-3, 5) RD 051000-4.

All tests were conducted at room temperature and the samples were handled with tweezers. Each test consisted of ten replicates.

Rupture Test

The rupture test was used to determine seal strength. Each capsule was placed in a plastic bag positioned with the seal of the capsule parallel to the probe and the flatter side down on a TA-90 heavy-duty platform. The test used a TA-4 probe, an acrylic cylinder, 1-½ inches in diameter, 35 mm tall. The test mode was Measure Force in Compression, return to start. The probe descended toward the sample at 2.0 mm/second until a trigger force of 15 grams was detected at which time data collection started. The probe returned at 10.0 mm/ second. The sample was compressed to 50 % of its' height at 2.0 mm/second.





The above graphs and the statistics below are each the average of ten tests replicates.

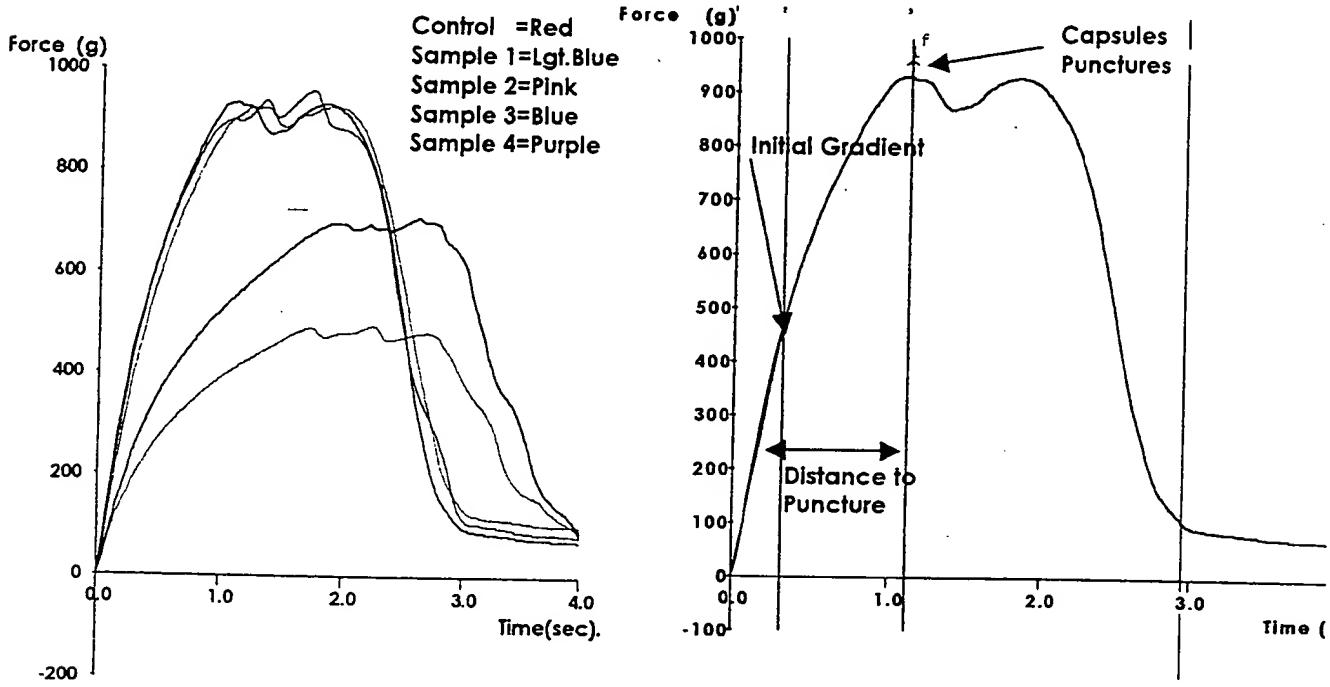
Sample	Control	1	2	3	4
Force to Rupture (g)	10,314	10,564	10,101	11,529	13,217
Gradient (g/s)	3,333	5753	5,143	4,262	6,061
Distance to Rupture (mm)	4.20	3.02	3.14	3.89	3.50

Observations:

The probe compressed the capsule 50% of its original height as determined by the instrument.
The capsule ruptured before the probe reached the target 50% strain.
Rupture is defined for this test when the capsule burst the seam.
The peak force was the point that the capsule ruptured.
After the capsule ruptured the force dropped off.

Puncture Test

The puncture test was to determine capsule strength. Each capsule was placed in a TA-302, a brass plate with ten 9-mm openings, positioned vertically with the flat side toward the bellows of the instrument and the more rounded side toward the probe. The test used a Needle like probe, 1-mm stainless steel probe. The test mode used was Measure Force in Compression, return to start. The probe traveled 2.0 mm/second until a trigger force of 2 grams was achieved at which point it penetrated vertically 10.0 mm into the capsule at a speed of mm/second. The probe withdrew 10.0 mm/second.



The above graphs and the statistics below are each the average of ten test replicates

Sample	Control	1	2	3	4
Force to Puncture (g)	545.0	965.3	985.7	799.8	976.7
Initial Gradient (g/s)	252.4	745.0	759.3	329.1	808.4
Distance to Puncture (mm)	4.41	2.60	2.69	4.92	2.42

Observations:

The needle-like probe was centered over the seam of the capsule.
The probe contacted the capsule and the force started to build as the probe compressed the sample.
The probe continued to travel to reach the target distance.
The capsule punctured with the needle-like probe.

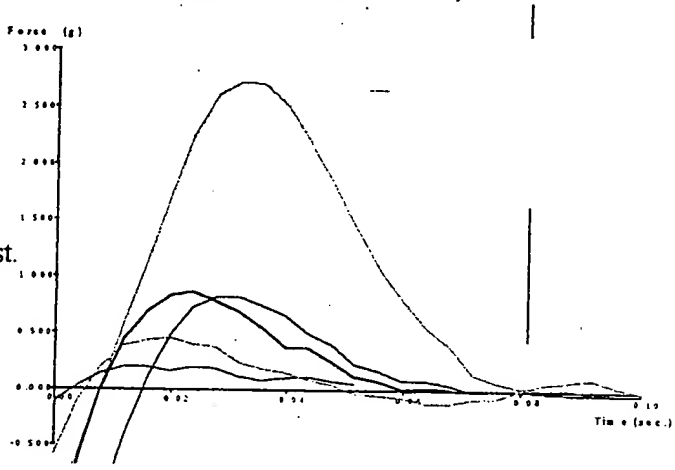
Adhesive Test

The adhesive test was used to determine the adhesive characteristics of the capsules. Two tests were conducted on the five samples. The first test was a capsule-to-capsule test. The capsules were placed in a TA-96, a stainless steel double grip. The capsules were placed in the grips such that their seams would touch when tested. The capsule in the upper grip traveled toward the capsule in the bottom grip at 0.5 mm/second. When a 5 gram trigger force was detected the sample traveled at 0.1 mm/second for a distance of 1 mm, held for 0.5 seconds under a load of 50 grams, then the upper grip returned at 0.5 mm/second

The second test performed was conducted under the same test parameters but with a TA-8, ¼" diameter stainless steel ball in the upper grip.

Sample	Control
Adhesive Peak Force (g)	1.0

The graph to the right and the above statistics are five Test replicates. Above data from capsule to capsule test.



Observations:

Data was unavailable for Samples 1-4 because there was not any adhesive characteristics to report for the capsule to capsule test.
Data unavailable for all samples for the probe to capsule test.

IVC INDUSTRIES, INC.
500 HALLS MILL ROAD I FREEHOLD, NEW JERSEY 07728 I PHONE: (732) 308-3000 FAX: (732) 761-2878

Alain Heron
ABT, LLC
852 Redgate Road
Dreshner, PA 19025-1431
FAX (215) 658-1222

September 15, 2000

Dear Alain:

You recently received Accelerated Stability Summary Reports of four (4) R&D batches of Vitamin E 400 Softgels. These R&D batches (RD 050100-1, 050400-2, 050800-3, and 051000-4) were each encapsulated using gelatin that had been reclaimed from the "scrap netting"of previous batches of Vitamin E Softgels using your Company's technology. The "history" of each of the batches is as follows:

- RD 050100-1 was encapsulated using gelatin that was reclaimed from the netting from Intergel production batch # 119228 of Vitamin E 400 Softgels.
- RD 050400-2 was encapsulated using gelatin that was reclaimed from RD 050100-1 netting.
- RD 050800-3 was encapsulated using gelatin that was reclaimed from RD 050400-2 netting.
- RD 051000-4 was encapsulated using gelatin that was reclaimed from RD 050800-3 netting.

At the completion of three (3) months accelerated stability, all test results were within specification for each of the above batches. Room Temperature Stability shall be continued over the next four (4) years.

From all of the above, it would appear that your Company's method of gelatin reclamation is a viable method of reducing raw material costs while still maintaining the quality of the resultant encapsulated product.

Sincerely,

William J. Neumann

William J. Neumann
Vice President
Quality and Regulatory Affairs

Room Temperature Stability Summary Report

PRODUCT NAME: *Vitamin E 400 IU Softgel Capsules*

PRODUCT CODE: *500031* **PRODUCT LOT#:** *119228*

PRODUCT DESCRIPTION: *Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.*

PACKAGE DESCRIPTION: *HDPE 175cc white (Mediaplast) bottle, closure, PP 33/400 neck with safeguard*

PRODUCT COUNT: *100 Capsules.*

ACTIVE INGREDIENT SUPPLIER (s):

Test Date:	INITIAL 05/00	6th Month 11/00	9th Month N/A	12th Month N/A	18th Month N/A

TEST	SPECIFICATION	METHOD	INITIAL	6ht Month	9th Month	12th Month	18th Month
Description	Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.	VISUAL	Compares to Standard.	Compares to Standard	N/A	N/A	N/A
Disintegration	NMT 45 minutes in a 0.05M acetate buffer.	USP <701>	Less than 15 minutes.	Less than 15 minutes.	N/A	N/A	N/A
Assay							
Vitamin E (dl-alpha Tocopheryl Acetate)	400 IU (95.0%-120.0%)	USP	409 IU (102.2%)	408 IU (102.0%)	N/A	N/A	N/A
Microbial Limits Total Plate Count	NMT 3000 per gram	USP	10 per gram	N/A	N/A	N/A	N/A
Combined Mold and Yeast	NMT 300 per gram		< 10 per gram	N/A	N/A	N/A	N/A
E.coli	Negative		Negative	N/A	N/A	N/A	N/A
Salmonella	Negative		Negative	N/A	N/A	N/A	N/A
Staphylococcus Aureus	Negative		Negative	N/A	N/A	N/A	N/A
Pseudomonas aeruginosa	Negative		Negative	N/A	N/A	N/A	N/A

Eric W. Sylvester / Date
Manager / Quality Control

Room Temperature Stability Summary Report

PRODUCT NAME: *Vitamin E 400 IU Softgel Capsules*

PRODUCT CODE: *500031* **PRODUCT LOT#:** *RD 050100-1*

PRODUCT DESCRIPTION: *Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.*

PACKAGE DESCRIPTION: *HDPE 175cc white (Mediaplast) bottle, closure, PP 33/400 neck with safeguard*

PRODUCT COUNT: *100 Capsules.*

ACTIVE INGREDIENT SUPPLIER (s):

Test Date:	INITIAL	6th Month	9th Month	12th Month	18th Month
	N/A	05/00	11/00	N/A	N/A

TEST	SPECIFICATION	METHOD	INITIAL	6th Month	9th Month	12th Month	18th Month
Description	Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.	VISUAL	Compares to Standard.	Compares to Standard	N/A	N/A	N/A
Disintegration	NMT 45 minutes in a 0.05M acetate buffer.	USP <701>	Less than 15 minutes.	Less than 15 minutes.	N/A	N/A	N/A
Assay							
Vitamin E (dl-alpha Tocopheryl Acetate)	400 IU (95.0%-120.0%)	USP	385 IU (96.2%)	384IU (96.0%)	N/A	N/A	N/A
Microbial Limits		USP					
Total Plate Count	NMT 3000 per gram		< 10 per gram	N/A	N/A	N/A	N/A
Combined Mold and Yeast	NMT 300 per gram		< 10 per gram	N/A	N/A	N/A	N/A
E.coli	Negative		Negative	N/A	N/A	N/A	N/A
Salmonella	Negative		Negative	N/A	N/A	N/A	N/A
Staphylococcus Aureus	Negative		Negative	N/A	N/A	N/A	N/A
Pseudomonas aeruginosa	Negative		Negative	N/A	N/A	N/A	N/A

Eric W. Sylvester 12/6/00

Eric W. Sylvester / Date

Manager / Quality Control

Room Temperature Stability Summary Report

PRODUCT NAME: *Vitamin E 400 IU Softgel Capsules*

PRODUCT CODE: *500031* **PRODUCT LOT#:** *RD 050400-2*

PRODUCT DESCRIPTION: *Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.*

PACKAGE DESCRIPTION: *HDPE 175cc white (Mediaplast) bottle, closure, PP 33/400 neck with safeguard*

PRODUCT COUNT: *100 Capsules.*

ACTIVE INGREDIENT SUPPLIER (s):

Test Date:	INITIAL	6th Month	9th Month	12th Month	18th Month
	05/00	11/00	N/A	N/A	N/A

TEST	SPECIFICATION	METHOD	INITIAL	6th Month	9th Month	12th Month	18th Month
Description	Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.	VISUAL	Compares to Standard.	Compares to Standard	N/A	N/A	N/A
Disintegration	NMT 45 minutes in a 0.05M acetate buffer.	USP <701>	Less than 15 minutes.	Less than 15 minutes.	N/A	N/A	N/A
Assay							
Vitamin E (dl-alpha Tocopheryl Acetate)	400 IU (95.0%-120.0%)	USP	384IU (96.0%)	389IU (97.2%)	N/A	N/A	N/A
Microbial Limits							
Total Plate Count	NMT 3000 per gram	USP	< 10 per gram	N/A	N/A	N/A	N/A
Combined Mold and Yeast	NMT 300 per gram		< 10 per gram	N/A	N/A	N/A	N/A
E.coli	Negative		Negative	N/A	N/A	N/A	N/A
Salmonella	Negative		Negative	N/A	N/A	N/A	N/A
Staphylococcus Aureus	Negative		Negative	N/A	N/A	N/A	N/A
Pseudomonas aeruginosa	Negative		Negative	N/A	N/A	N/A	N/A

Eric W. Sylvester 12/6/00

Eric W. Sylvester / Date

Manager / Quality Control

[redacted]

Room Temperature Stability Summary Report

PRODUCT NAME: *Vitamin E 400 IU Softgel Capsules*

PRODUCT CODE: *500031* **PRODUCT LOT#:** *RD 050800-3*

PRODUCT DESCRIPTION: *Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.*

PACKAGE DESCRIPTION: *HDPE 175cc white (Mediaplast) bottle; closure, PP 33/400 neck with safeguard*

PRODUCT COUNT: *100 Capsules.*

ACTIVE INGREDIENT SUPPLIER (s):

Test Date:	INITIAL 05/00	6th Month 11/00	9th Month N/A	12th Month N/A	18th Month N/A

TEST	SPECIFICATION	METHOD	INITIAL	6th Month	9th Month	12th Month	18th Month
Description	Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.	VISUAL	Compares to Standard.	Compares to Standard	N/A	N/A	N/A
Disintegration	NMT 45 minutes in a 0.05M acetate buffer.	USP <701>	Less than 15 minutes.	Less than 15 minutes.	N/A	N/A	N/A
Assay							
Vitamin E (dl-alpha Tocopheryl Acetate)	400 IU (95.0%–120.0%)	USP	382 IU (95.5%)	391 IU (97.8%)	N/A	N/A	N/A
Microbial Limits Total Plate Count	NMT 3000 per gram	USP	< 10 per gram	N/A	N/A	N/A	N/A
Combined Mold and Yeast	NMT 300 per gram		< 10 per gram	N/A	N/A	N/A	N/A
E.coli	Negative		Negative	N/A	N/A	N/A	N/A
Salmonella	Negative		Negative	N/A	N/A	N/A	N/A
Staphylococcus Aureus	Negative		Negative	N/A	N/A	N/A	N/A
Pseudomonas aeruginosa	Negative		Negative	N/A	N/A	N/A	N/A

Eric W. Sylvester 12/6/00

Eric W. Sylvester / Date
Manager / Quality Control

Ro m Temperature Stability Summary Report

PRODUCT NAME: *Vitamin E 400 IU Softgel Capsules*

PRODUCT CODE: *500031* **PRODUCT LOT#:** *RD 051000-4*

PRODUCT DESCRIPTION: *Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.*

PACKAGE DESCRIPTION: *HDPE 175cc white (Mediaplast) bottle, closure, PP 33/400 neck with safeguard*

PRODUCT COUNT: *100 Capsules.*

ACTIVE INGREDIENT SUPPLIER (s):

Test Date:			INITIAL 05/00	6th Month 11/00	9th Month 06/16/00	12th Month 07/17/00	18th Month 08/16/00
TEST	SPECIFICATION	METHOD	INITIAL	6th Month	9th Month	12th Month	18th Month
Description	Medium, oval shaped (7.5 minim), clear, pale yellow colored softgel capsules, which compares to the standard.	VISUAL	Compares to Standard.	Compares to Standard	N/A	N/A	N/A
Disintegration	NMT 45 minutes in a 0.05M acetate buffer.	USP <701>	Less than 15 minutes.	Less than 15 minutes.	N/A	N/A	N/A
Assay							
Vitamin E (dl-alpha Tocopheryl Acetate)	400 IU (95.0%-120.0%)	USP	389 IU (97.2%)	385 IU (96.2%)	N/A	N/A	N/A
Microbial Limits							
Total Plate Count	NMT 3000 per gram	USP	< 10 per gram	N/A	N/A	N/A	N/A
Combined Mold and Yeast	NMT 300 per gram		< 10 per gram	N/A	N/A	N/A	N/A
E.coli	Negative		Negative	N/A	N/A	N/A	N/A
Salmonella	Negative		Negative	N/A	N/A	N/A	N/A
Staphylococcus Aureus	Negative		Negative	N/A	N/A	N/A	N/A
Pseudomonas aeruginosa	Negative		Negative	N/A	N/A	N/A	N/A

Eric W. Sylvester / 12/6/00

Eric W. Sylvester / Date

Manager / Quality Control

Supporting Documentation For Paragraph 16 Of The Attached Response & Inventor Declaration

The Examiner's contention, and rejection, was that by employing the '408' patent, with a smaller pore size cartridge filter, one could achieve equivalent results as the present application in terms of residual oil removal.

Work done with smaller pore size cartridge filters, including smaller pore size than the tangential flow microfilters employed successfully in the present application, filed to remove the residual emulsified oils.

Index

Prefiltration Studies

Obj ctive: Determine if tighter prefiltration will improve microfiltration flux perfromance

M thod: Prepare 40 liters of 15% bone gelatin netting use 1 Kg netting & 2 Kg of DI water

Filter 15 liters of 15% Bone VitE netting (GNP) through a 1 or 10 micron polygard filter

Process the above filtered solution with a 0.5 m2 Durapore 0.65 micron v-screen cassette at 25/5 psi and ~ 55 degrees Celcius. Monitor permeate flow rates and permeate turbidity

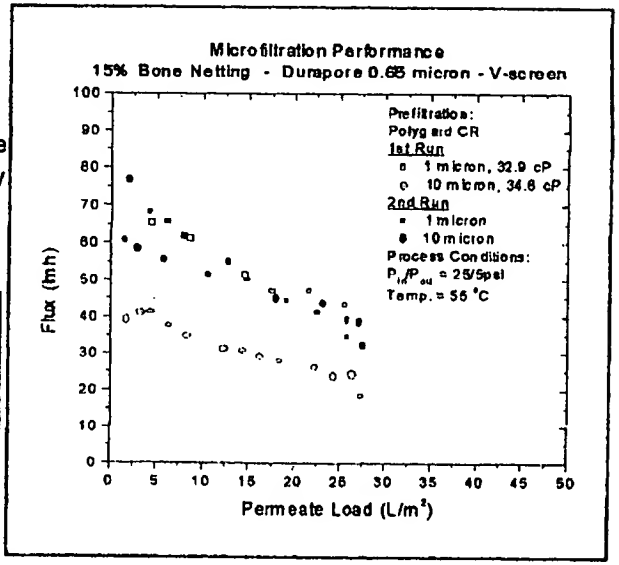
Results: & C nclutions:

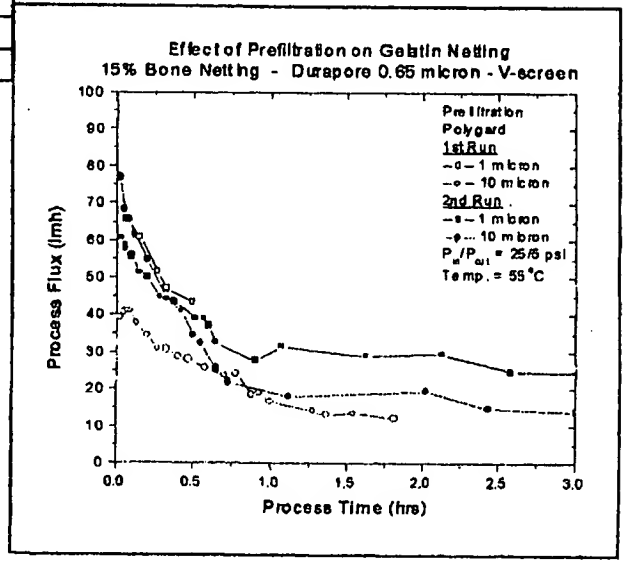
		Javg	Temp.	Viscocity	Turbidity	Total Solids
	Polugard	*lmh*	*°C*	*cP*	*NTU*	
Run 1	10 micron	48.0	52.8	35	189	20.88%
Run 2	10 micron	31.0	52.7		236	19.53%
Average		39.5	52.8	35	213	20.21%
Run 1	1 micron	51.2	52.5	33	109	20.79%
Run 2	1 micron	50.2	52.0		98	18.70%
Average		50.7	52.2	33	104	19.75%

The average process flux of the feed solutions prefiltered with 1 micron Polygard exibit higher process fluxes than the solutions prefiltered with 10 micron

Both pre-filters can be cleaned with hot water

The 10 micron filtrate turbidity is 2 times higher than the 1 micron filtrate.





Reccomendations:

1 micron Polygard filter is recommended for gelatin netting prefiltration

Clean filter with hot water after usgae

Roustness Study

Determine MIerformance for multiple process runs using staard cleaning cycles

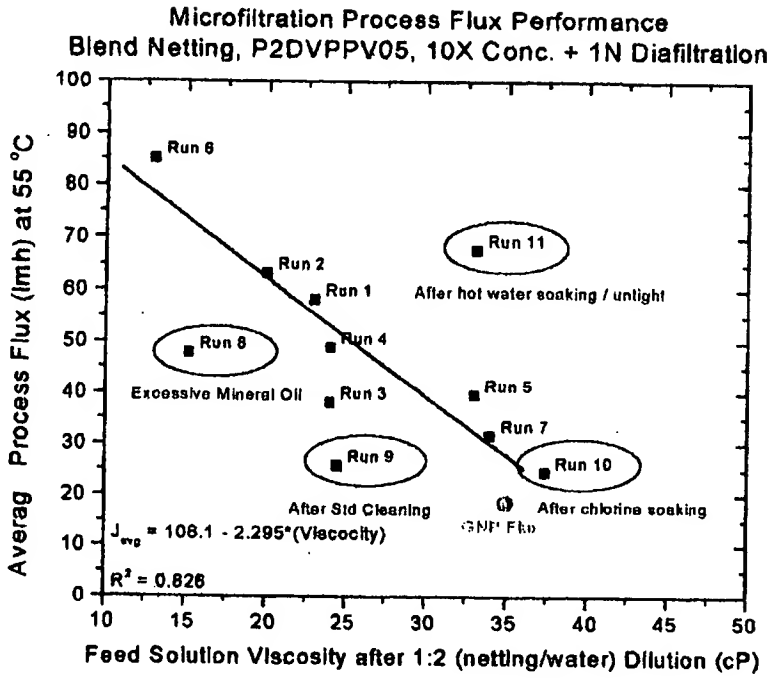
Feed Solution Operating Conditions:

- GNP Blend (de/Bone) netting
- 1 micron preration
- 10X Concention → 1N Diafiltration
- 40 L/m^2, 55 ‘25/5 psi

Measurementer Run:

- Process J_{avg}(jcess stability)
- Permeate Tudity, (permeate quality consistency)
- Gelatin Passe & Yield, (process economics)
- Clean H_w (chability)

Robustness Study Results



Conclusions:

- Permeate turbidity was acceptable for all runs
- The process flux is greatly influenced by the viscosity of the solution
- The normalized process flux was stable (average was 50 lmh/psi) with the exceptions of runs# 8 & 9
- The cleaning cycle is sufficient for process flux recovery. The lowest recommended value of the HWP prior to a run is 30 lmh/psi.
- The process flux AND cleanability are strongly influenced by the oil content - the higher the oil content the lower the flux and worse the cleanability.

	Javg	Feed Turb.	Perm Turb.	Total Solids	Gelatin	Glycerin	Passage	Yield	Viscocity	Water flux
	lmh	*NTU*	*NTU*	%	%	%			*cP*	lmh/psi
Average	47.9	120	37.07	17.84	11.73	6.11	0.928	0.953	25.56	52.5
Std. Dev.	18.65	36.74	4.19	1.84	1.253	0.998	0.051	0.008	8.0	16.6
min.	24.5	69	28	14.5	9.76	4.74	0.835	0.937	13	22.0
max	85	194	42	20.4	13.83	8.18	1.002	0.963	37.4	85.0

Microfiltration Robustness Study Summary of the Results

	Fouled Hw	Cleaned Hw1	Javg, 1st	Javg	Feed Turb.	Perm Turb.	Total Solids	Gelatin	Glycerin	Passage	Yield	Feed Viscocity
	lmh/psi	*lmh/psi*	*lmh*	*lmh*	*NTU*	*NTU*	%	%	%	%	%	*cP*
Initial Hw		*58.3*										
Run 1	17.0	47 / 62	58.1	22.5	113.0	33.9	17.4	12.0	5.43	92.3%	95.3%	23
Run 2	12.3	40 / 64	63.1	24.5	132.0	33.6	16.8	11.7	5.14	91.9%	95.2%	20
Run 3	15.8	39 / 59	38.0	14.7	194.0	40.2	19.2	12.0	7.2	84.9%	93.9%	24
Run 4	10.7	43 / 56	48.8	18.9	130.0	41.0	17.5	11.8	5.71	95.9%	95.8%	24
Run 5	16.4	35 / 48	39.6	15.3	110.0	36.9	20.4	13.8	6.57	95.9%	95.8%	33
Run 6	10.8	29 / 46	85.0	32.9	69.0	28.0	14.5	9.8	4.74	100.2%	96.3%	13
Run 7	11.3	32 / 44	31.6	12.2	171.0	37.5	19.8	13.4	6.41	94.3%	95.6%	34
Run 8	10.3	19 / 22	47.7	18.5	106.0	40.7	15.4	9.9	5.527	71.5%	90.6%	15.2
Run 9	7.0	19 /34	25.6	9.9	112.0	39.0	17.2	11.5	5.704	95.4%	95.7%	24.5
Run 10	15.4	23/85	24.5	9.5	108.0	42.0	19.1	10.9	8.185	83.5%	93.7%	37.4
run 11	51.0	65	64.9	25.1	75.0	35.0	18.9	12.3	6.588	93.6%	95.5%	33.1

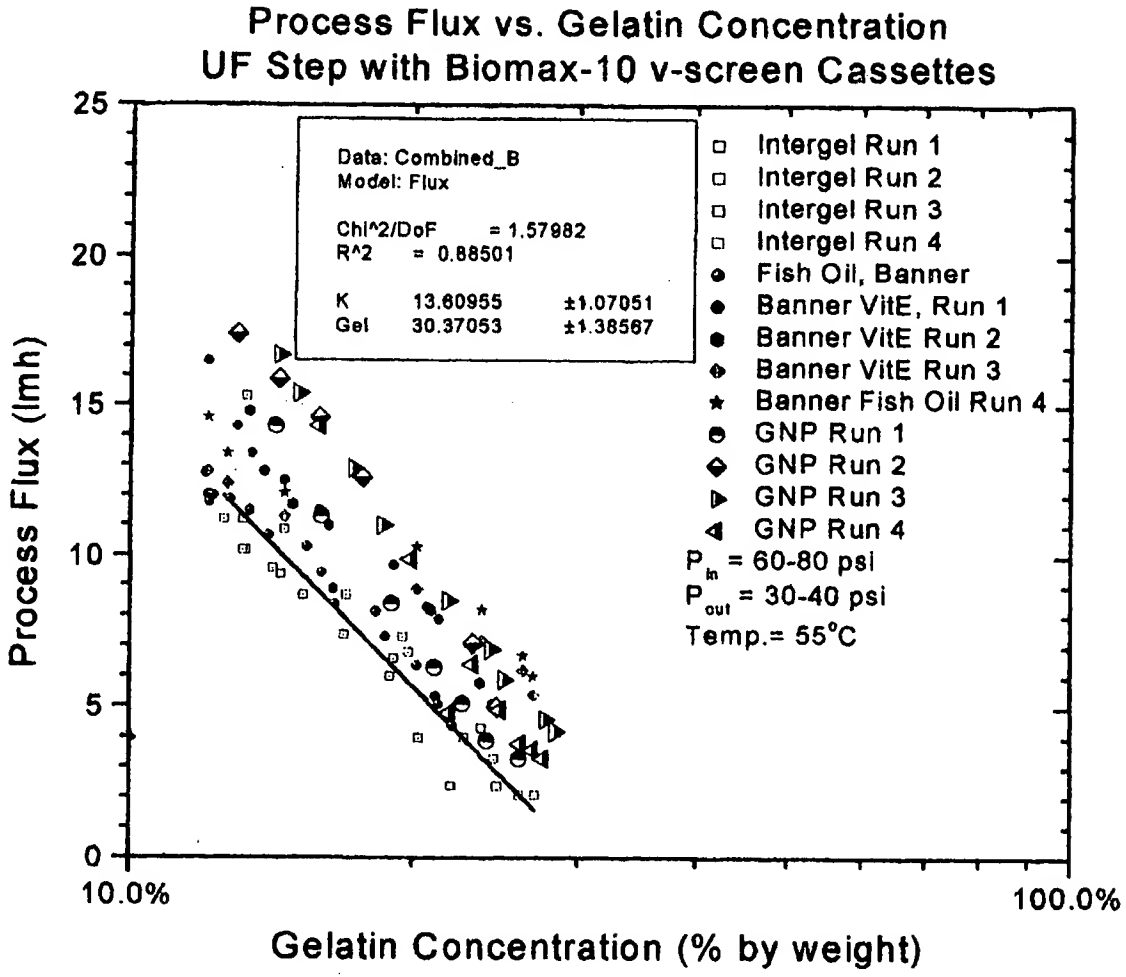
Notes 1. water flux measure after cleaning / water flux measured before next process run

2. Run 5 & 6, prefiltration was done using Polygard-10

avg flux 22.5 over 5 runs

intermediate cleaning 50% recovery

UF Performance Curves

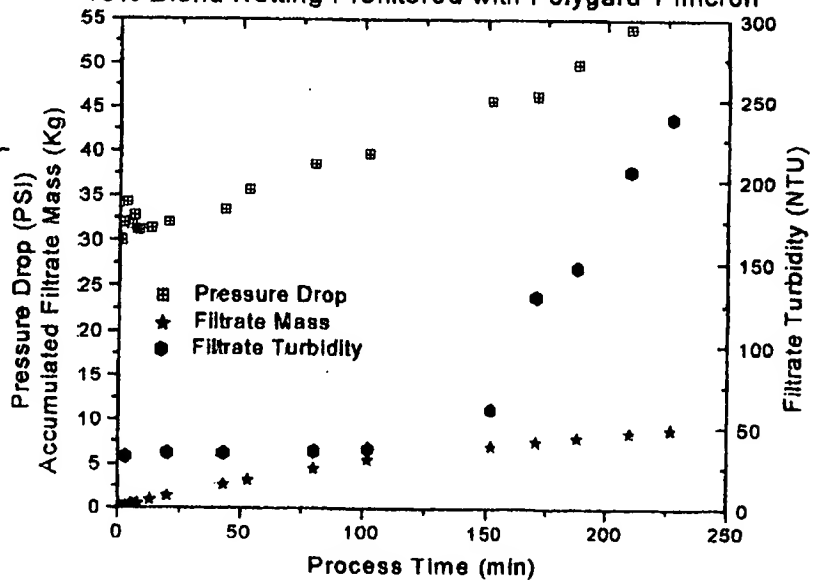


CRT-03 Evaluation

- **Objective:**
  - Evaluate a tight microfilter, Polygard CRT 0.3 micron, using gelatin waste netting.
- **Method:**
  - A 2" Polygard CRT cartridge
  - Initial Pressure = 50psi
  - Temp. = 55 °C
  - 15% Blend Netting prefiltered with Polygard 1micron
- **Measurements:**
  - Filtrate Flow Rate
  - Filtrate Turbidity
  - Inlet Pressure
- **Results:**

No of Batches per day	5
Process Time:	165 min
Filter Capacity DP per inch	4 Kg/inch
Filter Capacity Turb per inch	3.1 Kg/inch
Filter Rate:	0.037 Kg per min per inch

Figure 1. Prefiltration Performance - Polygard CRT03
15% Blend Netting Prefiltered with Polygard 1 micron



		Total Filter Length based on:			
Total Netting per day	Per Batch	Pressure	Turbidity	Flow Rate	Suggested Design
Kg	Kg	Inch	inch	Inch	
1500	300	375	484	50	49 x 10"
4500	900	1125	1452	149	148 x 10"
7500	1500	1875	2419	248	242 x 10"

Based on list price of $ 80 per 10" filter and 312 process runs per year, the annual cost of the Polygard CRT filters based on one and five usages is:

Total Netting Solution per Day	One usage	Five usages
1500 Kg	1223040	244608
4500 Kg	3644160	728832
7500 g	6040320	1208064

- **Conclusion:**

Due to the low filtrate throughput and early turbidity breakthrough, the number of the cartridges required for this application is very large and thus, the process cost becomes unrealistic. Even if we can clean the cartridges 5 times, the cost for the prefiltration / clarification step is more than 1.2 millions per year!

Supporting Documentation For Paragraph 18 Of The Attached Response & Inventor Declaration

The information in Section 4 demonstrates the ability of the present application to remove residual oils, of an aromatic nature, to undetectable levels, which cannot be achieved using the '408' patent.

The batch record is attached along with residual oil analysis (labeled as "Test #4 in section 4(b)) and 3 month accelerated stability results (labeled as "Trial #4 in section 4(c)).

A.B.T., L.L.C.

Pilot Manufacturing Directions
Gelatin Recovery
Batch No: TEST 4 - 8/16/00

Revision Date: 8/5/00
Revision: 1

Procedure

Initial & Date

1. Charge de-ionized water for netting dissolution to a clean, tared, previously inspected, appropriately sized, stainless steel tank (netting dissolution tank) equipped with a heating jacket variable speed mixer. AHP 8/15/00

Tank Size 600L

Tank No. GMR-17

Tank Tare Wt. 390.2 Kg

See new procedures @ 8/8/00

Charge 150kg netting first, then 300kg hot DI water.

De-ionized Water For Waste Netting Dissolution

	Charge #1	Charge #2	Charge #3
Gross Wt. (Kg)	840.8		
Tare Wt. (Kg)	540.2		
Net Wt. (Kg)	300.6		

Total Water Charged 300.6 Kg w/ Netting

2. Begin mild mixing and heat the water to 54°C ± 2°C (125°F-135°F). Maintain 54°C ± 2°C throughout the manufacturing process.

Mixer Type _____

Mixer No _____

Mixer On _____

RPM _____

Heating Start Time _____

Heating Stop Time _____

Initial Temperature _____ °C/°F

The netting was allowed to melt @ 135-140°F for 2hrs (5 → 7:00AM)

Then hot DI water (140°F) was added @ 7:00AM

→ The mixing started @ 9:00AM

Date Processed: _____ **Signature:** _____

Procedure **Initial & Date**

Final Temperature ~~____°C/°F~~ 59°C

PROCESS NOTE: It is important to maintain 54°C ± 2°C (125°F -135°F) through the manufacturing process. Temperatures above 56°C will accelerate degradation of the gelatin.

3. When the water has reached 54°C ± 2°C, charge the gelatin netting for dissolution while maintaining mild mixing.

Waste Netting For Dissolution

	Charge #1	Charge #2	Charge #3
Gross Wt. (Kg)	540.2		
Tare Wt. (Kg)	390.2		
Net Wt. (Kg)	150.0		

Total Netting Charged 150.0 Kg

Temperature Before Netting Charge Tank Setting 138°F °C/°F

Temperature After Netting Charge ____°C/°F

Netting Charge Start Time 5:00 → 7:05PM Melting

Netting Charge Finish Time 7:00 → 9:00PM Hot DI Water @ 138°F

Mixer On _____

RPM _____

Netting Type Used PS 3A NFNP Gel Batch No 10080056

Fish Oil Caps Batch 10080442 Fish Oil EP-321 PF

Date Processed:_____ **Signature:**_____

A.B.T., L.L.C.

Pil t Manufacturing Directions — **Revision Date: 8/5/00**
Gelatin Recovery — **Revision: 1**
Batch N :

Procedure — **Initial & Date**

Total Initial Mass in Dissolution Tank (Water + Netting) 450.6 Kg + 1.0 Kg Fish Oil (Spiked) AH 8/16/00

PROCESS NOTE: High mixing may result in the formation of a fine emulsion which is of sufficiently small size that it is either difficult to break and will not allow for efficient separation of the oil phase and/or residual oil.

4. Allow the netting to mix (mild mixing) for 30 minutes until all the gelatin netting has dissolved. Use a plastic or stainless steel rod to check for complete dissolution of the gelatin netting. If dissolution is not complete, mix an additional 15 minutes with mild mixing. Repeat if necessary

Hand mixing was easier than Vit E netting (may be due to 3A Gel formula @ 41% Gelatin vs 2A Gel Formula @ 43.5% Gelat.)

Initial Temperature 59 °C/°F

Final Temperature 56.3 °C/°F

Mixing Start Time 9:00 PM

Mixing Stop Time 9:50 PM

RPM Hand mixing + mixer 30

Complete dissolution & homogenization in 50 mins!

Dissolution Complete ✓ YES (proceed step #5) _____ NO (continue mixing)

Initial Temperature _____ °C/°F

Final Temperature _____ °C/°F

Mixing Start Time _____

RPM _____

Mixing Stop Time _____

Dissolution Complete _____ YES (proceed step #5) _____ NO (continue mixing)

Date Processed:_____ **Signature:**_____

Procedure — **Initial & Date**

5. While dissolution of the gelatin netting is in progress, preheat the TFF filtration unit to 52°C ± 2°C (125°F ± 4°F) by circulating hot process water through the unit until the completion of the skimming and pre-filtration . Determine the system hold-up volume during this preheating step.

Initial Outlet Temperature 50 °C

Final Outlet Temperature 50 °C

Heat Exchanger Settings @ 50°C

Circulation Start Time _____

Circulation Stop Time _____

System Hold-Up Volume ~ 90 Kg
(for mass balance calculations)

PROCESS NOTE: It is important to preheat the filtration unit to avoid potential congealing of the aqueous gelatin layer.

6. When dissolution of the gelatin netting is complete, stop mixing and allow the mixture to stand for 60 minutes minimum for the gross separation of the oils.

Mixer Off ✓

Hold Start 9:50 PM

Hold Stop 1:00 AM

Initial Temperature 56.3 °C

Final Temperature 54.5 °C

Oil Layer is clear but containing greenish floating pieces → Fish oil smell.

Interface clear & neat.

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

7. Collect 2 ounce samples (pre-skimming) from the dissolution tank for residual oil analysis.

   Samples Collected

   Yes _____

   No _____

8. Using a skimmer, previously cleaned and inspected, remove the separated, upper oil layer to a previously cleaned, tared, appropriately sized collection container. Approximately 60 – 90 minutes will be required to complete oil removal from the surface.

   Skimming Start Time _____

   Skimming Stop Time _____

   Initial Temperature _____ °C/°F

   Final Temperature _____ °C/°F

   Oil Collected Gross Wt. _____ Kg

   Tare Wt. _____ Kg

   Net Wt. _____ Kg

No skimming step replaced by careful visual, physical separation.

9. If appropriate, separate the oil layer collected in Step #7 and obtain weights of the aqueous and oil layers and sample of the aqueous layer for analysis and mass balance calculations.

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

Oil Layer Collected Gross Wt. _____Kg

Tare Wt. _____Kg

Net Wt. _____Kg

Aqueous Layer Collected Gross Wt. _____Kg

Tare Wt. _____Kg

Net Wt. _____Kg

10. Prepare a clean, tared, previously inspected, appropriately sized, stainless steel tank (Millipore TFF unit- MF feed tank) equipped with a heating jacket and variable speed mixer. Preheat the tank to 52°C ± 2°C (125°F ± 4°F).

Tank Size _____ Millipore MF Feed Tank

Tank No. _____

Tank Tare Wt. _____Kg

Tank Temperature _____°C/°F Heat Exchanger Setting @ 50°C

11. Pre-filter the post-skimmed contents of the dissolution tank, via a 10 micron cartridge filter, to the tank of Step #10.

Dissolution Tank Initial Temperature 54.5 °C/F

Pre-filtration Start Time 1:25 AM

Pre-filtration Stop Time 1:35 AM

Microfiltration Feed Tank Final Temp. 56.1 °C/F

10μ.

Heat Tape to avoid Gel Plug -

Date Processed:_____ **Signature:**_____

A.B.T., L.L.C.

Pilot Manufacturing Directions — **Revision Date: 8/5/00**
Gelatin Recovery — Revision: 1
Batch No:

Procedure — **Initial & Date**

Microfiltration Feed Mass

Height Conversion → Volume → Mass

Tank No. _____

~~Tank Gross Wt.~~ _____ Kg

~~Tare Wt~~ _____ Kg

Net Wt. _____ Kg

Initial Height: 82.3

w/ circulation H: 79.8

ρ: 1.00?

Actual = 437L = 437kg.

Dissolution Tank Residual Mass

Tank No. GMR-17

Tank Gross Wt. 407.6 Kg

Tare Wt. 390.2 Kg

Net Wt. 17.4 Kg

Appearance
2/3 Gelatin @ 13% →
1/3 oil

Oil Layer composite sample Collected

Theoritical 450.6 - 17.4 = 433.2 kg in MF Feed Tank -

12. Collect 2 ounce samples **(pre-MF)** from the MF feed tank, after skimming and pre-filtration, for residual oil analysis. _____

Samples Collected

Yes ✓

No _____

Date Processed: _____ **Signature:** _____

Procedure **Initial & Date**

13. Prepare a clean, tared, previously inspected, appropriately sized, stainless steel tank (Millipore TFF unit- MF permeate / UF retentate tank) equipped with a heating jacket and variable speed mixer. Preheat the tank to 52°C ± 2°C (125°F ± 4°F). AH 8/16/00

~~Tank Size~~ Millipore UF Feed Tank

~~Tank No.~~ Settings @ 55°C

~~Tare Tank Wt.~~ ~~Kg~~

Tank Temperature _____ °C/°F

14. Turn on the preheated filtration unit and begin microfiltration to remove residual oil contamination. At the predetermined concentration of the feed solution, add one volume of process water and diafilter the feed solution to maximize gelatin & glycerin throughput. Collect the microfiltration permeate in the tank described in Step #13.

Membrane Pore Size 0.65µ

Membrane Lot# # lots

Membrane Surface Area 4.5 sq m.

Process Flow Rate _____

Microfiltration Start Time 1.50 recirculation

Diafiltration Start Time 3:35 concentration
~~4:20~~ diafiltration

Water for Diafiltration Gross ~~Kg~~

~~Tare~~ ~~Kg~~

Net 72 Kg

Temp. 55 °C/~~F~~

			concentration	diafiltration	
Time	1:50	3.05	3:35	4:20	4:35
Feed	95.6				
Permeate NTU	36.4				
Flow Rate l/min	6.95	5.7	5.1	4.4	3.65
T °C	56.5	54.1	53.1	54.4	55.5

composite permeate 39.9
last permeate 30.2

Target Height → 1.3 end of concentration 6x

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

Microfiltration Finish _____ AH 8/16/00

Flux Rates see attached

Transmembrane Pressures see attached See previous table

Process Temperature During Microfiltration (30 minute intervals)

Time								
Temp, °C								

15. Collect 2 ounce **samples (post-MF)** from the MF permeate/ UF retentate tank for residual oil analysis.

Samples Collected

Yes ✓

No _____

16. Weigh the MF feed tank to determine the mass of unprocessed material (MF retentate). Collect a 2 ounce **sample (MF retentate)** for water and glycerin analysis for mass balance calculations. Make the assumption that the material in the hold-up volume is of the same composition as this sample.

Residual Microfiltration Tank # Millipore MF Feed Tank

Gross Wt. _____ Kg

Tare Wt. _____ Kg

Net Wt. _____ Kg

Height: 1.3 ie 72kg

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

17. Weigh the MF permeate / UF retentate tank and hold at 52°C ± 2°C (125°F ± 4°F) while preparing for ultrafiltration. AH 8/16/00

Microfiltration Permeate Tank # 2 Millipore UF Feed tank

Gross Wt. 2 _____ Kg

Tare Wt. 2 _____ Kg

Net Wt. _____ Kg

Hold Start _____

Initial Temp _____ °C/°F

Hold Finish _____

Final Temp _____ °C/°F

Initial Height - 78
w/ circulation 77.2

ρ = 1.00

Actual = 432 kg

18. Clean the microfiltration unit using the procedure described below. Monitor the cleanability of the membrane (see attached membrane cleaning/regeneration data).

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

AH 8/16/00

19. Preheat the ultrafiltration unit to 52°C ± 2°C (125°F ± 4°F) by circulating hot process water through the unit for 15 minutes. OK.

    Initial Outlet Temperature _____°C/_°F @ 55°C

    Final Outlet Temperature _____°C/°F

    Circulation Start Time _____

    Circulation Stop Time _____

PROCESS NOTE: It is important to preheat the filtration unit to avoid potential congealing of the aqueous gelatin layer being transferred.

20. Prepare a clean, tared, previously inspected, appropriately sized, stainless steel tank (UF permeate tank).

    Tank Size 500L

    Tank No. 1215

    Tank Tare Wt _____ Kg

    Tank Temperature _____ °C/°F

Procedure **Initial & Date**

21. Turn on the preheated filtration unit and begin ultrafiltration to concentrate the feed solution to the desired concentration of gelatin for recycle.

Membrane Pore Size: 10K

Membrane Lot#: ≠ lot

Membrane Surface Area: 11 sqm

Process Flow Rate: _____

Concentration Start Time: 4:50 AM

Concentration Finish Time: 6:45 AM

Flux Rates: see ~~attached~~ table

Transmembrane Pressures: see ~~attached~~

Problem: Three times in a row, the UF Pump overheating limiting the UF concentration. We stopped @ 6:45 AM while we were still > 5 lmh. At Integral Millipore said that we can run as low as 2 lmh!

→ We reached 36.7% recycle ⇒ We can easily reach 40% recycle

Process Temperature (feed tank) During Concentration (30 minute intervals)

Time	4:50	5:35	6:00	6:15	6:30	6:45		
Temp, °C	53.9	61.7	62	62.3	61.9	61.2		
Flow Rate	2.85	2.4	2.1	1.64	1.4	1.3		
Weight	77.2	48	36.5	30.5	28	27		

22. When concentration is complete, weigh the MF permeate / UF retentate tank. Maintain 52°C ± 2°C (125°F ± 4°F) while analysis is in progress.

~~Tank No.~~ _____ Transfer into Gel Tank

Tank Gross Wt. 477.5 Kg

Tare Wt. 273.5 Kg

Net Wt. 204.0 Kg

GNP or next Trials @ 35%/min Trying to reach 40% @ each recycle.

Pump — 460V vs 230V GNP utility allowing > 30 amp

Date Processed: _____ **Signature:** _____

Procedure **Initial & Date**

23. When concentration is complete, weigh the UF permeate tank and collect 2 ounce samples (UF permeate) for water & glycerin analysis for mass balance determination.

Samples Taken

Yes ✓

No _____

Tank No. _____

Tank Gross Wt. _____ Kg

Tare Wt. _____ Kg

Net Wt. 217.2 Kg

Retentate 204
Permeate 217.2
Hold Up ~10g

24. When concentration is complete, obtain 4-ounce samples (UF retentate) from the MF permeate / UF retentate tank for duplicate water analysis by LOD and duplicate glycerin analysis by GPHPLC, RI Detector or ELSD. Maintain 52°C ± 2°C (125°F ± 4°F) while analysis is in progress.

Water & Glycerin Analysis

LOD (%H2O)	GPHPLC (Glycerin)
Analysis #1 65.17	Analysis #1
Analysis #2 64.91 #3 65.88	Analysis #2
Average LOD 65.3%	Average 6.9%

→ 27.8% Gelatin

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

See attached Banner calculations

25. Based on the analysis in Step #24, determine the quantities of virgin gelatin and glycerin required to proceed to gel mass production with _____% recycled gelatin and _____% recycled glycerin and subsequent capsule manufacturing.

Virgin Gelatin Requirement _____

Virgin Glycerin Requirement _____

Calculation: Glycerin from previous gel mass – COA water content _____

Lot No. _____

Gelatin from previous gel mass – COA water content _____

Lot No. _____

Calculation:

a. Glycerin Assay (average from Step #23) / COA Assay = Actual Glycerin Content in Final Concentrated Gel Mass

b. Actual Gelatin Content in Final Concentrated Gel Mass =
Gelatin anhydrous Content/Gelatin purity
i.e.
(100 - Water -Glycerin Assay (a. above) / (100 - Gelatin Water Content/100)

Procedure **Initial & Date**

c. Actual Water Content in Final Concentrated Gel Mass = 100% - (a. and b. above)

d. Combination Gel Mass preparation
Total Gel Mass (kg) = Actual Water Content (kg) / Gel Mass Water Content (%)

Total Gelatin (kg) = Total Gel Mass (kg) x Gel Mass Gelatin Content (%)

Virgin Gelatin (kg) = Total Gelatin (kg) – Actual Gelatin (kg) (b. above)

Total Glycerin (kg) = Total Gel Mass (kg) x Gel Mass Glycerin Content (%)

Virgin Glycerin (kg) = Total Glycerin (kg) - Actual Glycerin (kg) (a. above)

e. Percentage recycle

Gelatin Recycle (%) = Actual Gelatin (kg)/ Total Gelatin (kg) $\frac{56.7}{155.2} = 36.5\%$

Glycerin Recycle (%) = Actual Glycerin (kg)/ Total Glycerin (kg) $\frac{14.1}{83.7} = 16.8\%$

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

26. Determine a mass balance on the completed process.
    - Water

    a. Water input
        i. System hold-up _____
        ii. From netting input _____
        iii. Initial dissolution volume _____
        iv. Microfiltration diafiltration volume _____
            1. Total water input _____

    b. Water out
        i. Residual from microfiltration feed tank _____
        ii. Excess from oil skimmer operation _____
        iii. Concentration permeate _____
        iv. In final concentrated retentate _____
            1. Total water accounted for _____

    c. Water mass balance (water out / water input) _____

A.B.T., L.L.C.

Pilot Manufacturing Directions — **Revision Date: 8/5/00**
Gelatin Recovery — **Revision: 1**
Batch No:

Procedure — **Initial & Date**

- Gelatin

a. Gelatin input
   1. From netting input — $150_{kg} \times .417 = 62.55_{kg}$

b. Gelatin out
   1. Residual from microfiltration feed tank — _____
   2. From oil skimmer operation — $17.4_{kg} \times 2/3 \times 13\% \rightarrow 1.508_{kg}$
   3. Concentration permeate — _____
   4. In final concentrated retentate — $204_{kg} \times .278 = 56.712_{kg}$

c. Total gelatin accounted for — _____

d. Gelatin mass balance (gelatin out / gelatin input) — _____

- $\frac{56.712}{62.55} = 90.67\%$ Yield.
- $\frac{56.712 + 1.509}{62.55} = 93.07\%$ Yield better physical separation
- 5.8 kg Oil $\Rightarrow 150 - 5.8 = 144.2$ kg Netting $\times .417 = 60.1314$ kg

$\frac{56.712}{60.1314} = 94.3\%$ $\frac{58.22}{60.1314} = 96.8\%$ ← better separation

Date Processed:_____ **Signature:**_____

Procedure **Initial & Date**

- Glycerin input
  a. From netting input _____

  b. Glycerin out
    1. Residual from microfiltration feed tank _____
    2. From oil skimmer operation _____
    3. Concentration permeate _____
    4. In final concentrated retentate _____

  ii. Total glycerin accounted for _____

- Glycerin mass balance (glycerin out / Glycerin input) _____

27. Attachments
    - Flux Profiles
    - Pressure profiles
    - Membrane cleaning/regeneration profiles
    - QC analysis sheets

Clean the filtration unit using the procedure described below. Monitor the cleanability of the membrane (see attached membrane cleaning/regeneration data).

Date Processed:_____ **Signature:**_____

Gel Mass Calculation for Millipore Gel Netting Filtration Samples
3A Formula

0.1 used fish netting. L. Ikeuchi E-19.

1. Filtered Gel/Water (F G/W) solution weight: 204.0 kg Lot # Made 8/16/2000
2. Glycerol % in F G/W solution: 6.9 % (from QC results)
3. Water % in F G/W solution: 65.3 % (from TS results)
4. Gel Powder % in F G/W solution:

$$100 - \underset{\text{(Glycerol \% step 2)}}{6.9} - \underset{\text{(Water \% step3)}}{65.3} = 27.8 \text{ \% Gel Powder}$$

5. 3A Formula Requirement

	3A %
Gelatin Powder:	41.700
Glycerin:	22.500
Water:	35.800

6. Total quantity of gel mass that can be made
   a. Weight of Water in F G/W: (Water % (step3) x 0.01) x Wt of F G/W (step1) =
   0.653 x 204.0 = 133.2 kg of water
   b. Wt of water in F G/W divided by 3A water % = Total quantity of 3A gel mass

$$\frac{\text{(Step 6a.)}}{\text{(\% Water in 3A (step5) x .01)}} = \frac{133.2}{0.358} = 372.1 \text{ kg of 3A gel mass}$$

7. Gelatin Powder and Glycerin Requirements for 3A Mass
   a. Total kg 3A mass = 372.1 (from step 6b.)
   b.

		3A %	Kg of New Mass Requires
i.	Gelatin Powder:	41.700	(0.417 x (step 7a.) = .417 x 372.1 = 155.2
ii.	Glycerin:	22.500	(0.225 x (step 7a.) = .225 x 372.1 = 83.7
iii.	Water:	35.800	(step 6a.) 133.2

Gel Mass Calculation for Millipore Gel Netting Filtration Samples
3A Formula

8. Gelatin and Glycerin Quantities in F G/W solution

		F G/W solution (kg)
a. Gelatin Powder: ((% Gelatin (step4) x 0.01) x (step 1))	= 0.278 x 204.0	= 56.7
b. Glycerin: ((% Glycerol (step2) x 0.01) x (step 1))	= 0.069 x 204.0	= 14.1
c. Water: (from step 6a.)	= 133.2	

9. Required Quantities of Gelatin and Glycerin for Making Next 3A Gel Mass

	3A Formula	From F G/W	
a. Gelatin Powder:	155.2 (step 7bi) -	56.7 (step 8a) =	98.5 kg
b. Glycerin:	83.7 (step 7bii) -	14.1 (step 8b) =	69.6 kg
c. Water:	133.2 (step 7biii) -	133.2 (step 8c) =	0.0 kg

Meilin Mak
Calculated By

8/16/2000
Date

BANNER
Omnimark Instrument Corp

Operator:
Sample #: 1
Program 4: FILTRATE
UNITS: MOISTURE
TEMP1: 140C TIME1: 8.0 MINUTES
TEMP2: 100C TIME2: OFF
SLOPE: WINDOW: 0.2 %IW: 0.100
STANDBY:125C IDEAL WT: 6.0

Time	Temp	Weight	Data	Unit
0:00	119C	5.627	0.00%	M
1:00	140C	5.437	3.38%	M
2:00	140C	5.033	10.56%	M
3:00	140C	4.642	17.50%	M
4:00	140C	4.366	22.41%	M
5:00	140C	4.069	27.33%	M
6:00	140C	3.825	32.02%	M
7:00	140C	3.583	36.32%	M
8:00	140C	3.362	40.25%	M
9:00	125C	3.194	43.24%	M
10:00	107C	3.087	45.14%	M
11:00	101C	3.007	46.56%	M
12:00	101C	2.923	48.05%	M
13:00	100C	2.840	49.53%	M
14:00	100C	2.757	51.00%	M
15:00	100C	2.676	52.44%	M
16:00	100C	2.598	53.83%	M
17:00	100C	2.524	55.14%	M
18:00	100C	2.454	56.39%	M
19:00	100C	2.387	57.58%	M
20:00	100C	2.325	58.68%	M
21:00	100C	2.267	59.71%	M
22:00	100C	2.214	60.65%	M
23:00	100C	2.164	61.54%	M
24:00	100C	2.117	62.38%	M
25:00	99C	2.074	63.14%	M
26:00	100C	2.032	63.89%	M
27:00	100C	1.994	64.56%	M

RESULT on 16 AUG 2000 at 7:56:13
ELAPSED TIME: 27:59

65.17% M

INITIAL WEIGHT = 5.627 grams
FINAL WEIGHT = 1.960 grams
WEIGHT LOSS = 3.667 grams

BANNER
Omnimark Instrument Corp

Operator:
Sample #: 1
Program 4: FILTRATE
UNITS: MOISTURE
TEMP1: 140C TIME1: 8.0 MINUTES
TEMP2: 100C TIME2: OFF
SLOPE: WINDOW: 0.2 %IW: 0.100
STANDBY:125C IDEAL WT: 6.0

Time	Temp	Weight	Data	Units
0:00	111C	5.600	0.00%	M
1:00	132C	5.438	2.89%	M
2:00	141C	5.029	10.20%	M
3:00	140C	4.639	17.16%	M
4:00	140C	4.352	22.29%	M
5:00	140C	4.071	27.30%	M
6:00	140C	3.801	32.12%	M
7:00	140C	3.547	36.66%	M
8:00	140C	3.304	41.00%	M
9:00	126C	3.121	44.27%	M
10:00	109C	3.001	46.41%	M
11:00	99C	2.914	47.96%	M
12:00	99C	2.824	49.57%	M
13:00	100C	2.733	51.20%	M
14:00	100C	2.645	52.77%	M
15:00	100C	2.559	54.30%	M
16:00	100C	2.478	55.75%	M
17:00	100C	2.401	57.13%	M
18:00	100C	2.329	58.41%	M
19:00	99C	2.264	59.57%	M
20:00	100C	2.205	60.63%	M
21:00	100C	2.150	61.61%	M
22:00	100C	2.100	62.50%	M
23:00	100C	2.054	63.32%	M
24:00	100C	2.012	64.07%	M
25:00	100C	1.975	64.73%	M

RESULT on 16 AUG 2000 at 8:23:54
ELAPSED TIME: 25:19

64.91% M

INITIAL WEIGHT = 5.600 grams
FINAL WEIGHT = 1.965 grams
WEIGHT LOSS = 3.635 grams

BANNER
Omnimark Instrument Corp

Operator:
Sample #: 1
Program 4: FILTRATE
UNITS: MOISTURE
TEMP1: 140C TIME1: 8.0 MINUTE
TEMP2: 100C TIME2: OFF
SLOPE: WINDOW: 0.2 %IW: 0.100
STANDBY:125C IDEAL WT: 6.0

Time	Temp	Weight	Data	Un
0:00	106C	5.633	0.00%	M
1:00	126C	5.538	1.69%	M
2:00	139C	5.167	8.27%	M
3:00	140C	4.774	15.25%	M
4:00	140C	4.491	20.27%	M
5:00	140C	4.219	25.10%	M
6:00	140C	3.954	29.81%	M
7:00	140C	3.697	34.37%	M
8:00	140C	3.458	38.61%	M
9:00	126C	3.280	41.77%	M
10:00	109C	3.155	43.99%	M
11:00	99C	3.063	45.62%	M
12:00	100C	2.975	47.19%	M
13:00	100C	2.883	48.82%	M
14:00	100C	2.793	50.42%	M
15:00	100C	2.704	52.00%	M
16:00	100C	2.620	53.49%	M
17:00	100C	2.541	54.89%	M
18:00	100C	2.465	56.24%	M
19:00	100C	2.394	57.50%	M
20:00	100C	2.328	58.67%	M
21:00	100C	2.266	59.77%	M
22:00	100C	2.207	60.82%	M
23:00	100C	2.155	61.74%	M
24:00	100C	2.105	62.63%	M
25:00	100C	2.061	63.41%	M
26:00	100C	2.020	64.14%	M
27:00	100C	1.981	64.83%	M
28:00	100C	1.944	65.49%	M

RESULT on 16 AUG 2000 at 8:47:12
ELAPSED TIME: 28:40

65.88% M

INITIAL WEIGHT = 5.633 grams
FINAL WEIGHT = 1.922 grams
WEIGHT LOSS = 3.711 grams

Average: 65.3

nm 8/16/2000

TECHNICAL SERVICES
TEST REQUISITION

№ 4656

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REQUEST TYPE:

___ QC RAW MATERIAL ANALYSIS
___ QC FINISHED PRODUCT ANALYSIS
___ NEW PRODUCT FORMULATION
___ GELATIN COLOR FORMULATION
___ PHARMACEUTICAL FORMULATION
___ VENDOR EVALUATION
___ MAINTENANCE/CALIBRATION
✓ OTHER Mineral residue in gelatin

SAMPLE CONTROL # N/A
SAMPLE CODE # N/A
OTHER Reagents Gel
QUANTITY SUBMITTED
DATE SUBMITTED
REQUESTED COMPLETION DATE

****

TEST DESCRIPTION: Mineral residue in gelatin mass per AB Technologies test method

REQUESTED BY: LEE Ikemoto

TEST RESULTS:

	Test 1	Test 2	Test 3	Test 4
UF Retentate	0.003%	0.001%	0.001%	0.003%
Post-UF layer	0.006%	0.007%	0.014%	0.003%
Pre-UF layer	0.025%	0.010%	0.048%	0.009%
	0.166%	0.449%	0.394%	0.243%

(XT-264)

DOCUMENTS ATTACHED: Chromatograms PAGES

COMPLETED BY: [signature] DATE: 11/14/2000

VERIFIED BY: [signature] DATE: 11/14/2000

White - Test Requisition File
Yellow - Product/Customer File
Pink - Requestor's with Data
Goldenrod - Requestor's Copy

Physical stability on capsules made in August, using Reclaimed Gel.

Code	Control #	14 days Accelerated	1 month Accelerated	2 Months Accelerated	3 Months Accelerated	3 Months Bulk RT
E-1182PF	10080250 Main	Not Tested	Stuck together; bottle bottom removed to remove and break up capsules one by one. After breaking up has remained as individual, does not reclump back. 0/100 leakers.	Capsules were soft and stuck together. Removed the bottom of the bottle and broke up the capsules one by one. After braking up the capsules remained as individuals. No leakers were found.	Pass. No leakers were found.	Pass. No leakers were found.
E-1182PF	10080250A Sublot	Some stuck together, and slight deformity, can be removed from bottle. 0/100 leaker	Soft, stuck together; bottle bottom removed to remove and break up capsules one by one. After breaking up has remained as individuals does not reclump back. 0/100 leaker	The physical evaluation showed no difference between the main lot and the sublot manufactured using the reclaimed gel. No leakers were found.	Pass. No leakers were found.	Pass. No leakers were found.
E-1182PF	10080251 Main	Not Tested	Not tested	Pass. No leakers were found.	Pass. No leakers were found.	Pass. No leakers were found.
E-1182PF	10080251A Sublot	Pass. 0/100 leakers.	Pass. 0/100 leakers.	Pass. No leakers were found.	Pass. No leakers were found.	Pass. No leakers were found.
EP-321PF	10080056 Main	Soft, slight deformity 0/50 leaker	2 caps deformed and very soft; one capsule melted 0/50 leaker	Capsules were stuck together. Removed the bottom of the bottle and broke up the capsules one by one. Brown spots were observed on the bottom and the sides of the bottle, and on the surface of 23 capsules (dried oxidized fill material). Found one capsule leaking (half empty). The gelatin shell of 23 capsules out of 50 had melted contact spots.	Capsules were stuck together. Removed the bottom of the bottle and broke up the capsules one by one. Brown spots were observed on the bottom and the sides of the bottle, and on the surface of o 40 out of 50 capsules (dried oxidized fill material).The gelatin shell of 40 capsules out of 50 had melted spots Capsules were leaking from the melted spots of the shell.	Pass. No leakers were found.
EP-321PF	10080056A Sublot	Deformed, gel melted looks like heat induced problem. 3/50 leakers	Soft, deformed, stuck in bottle, shell not melted like 14 day sample. 1/50 leaker	The physical evaluation showed no difference between the main lot and the sublot manufactured using the reclaimed gel. Brown spots were observed on the surface of 19 capsules. 1/50 was leaking. The gelatin shell of 19 capsules out of 50 had melted contact spots.	The physical evaluation showed no difference between the main lot and the sublot manufactured using the reclaimed gel. Brown spots were observed on the surface of 30 capsules. 1/50 was leaking. The gelatin shell of 30 capsules out of 50 had melted contact spots.	Pass. No leakers were found.
L-166PF	TS-0068 Main	Normal. 0/60leakers	Normal. 1/60 leakers(air bubbles in shell)	Some capsules were deformed. Capsules were oily from leakers .1/60 was leaking. The capsule was leaking from the melted spot not the seem.	1/60 leaking. Some capsules were deformed. Capsules were oily from the leaking fill material . The capsule was leaking from the melted spot not the seam.	Pass. No leakers were found.
L-166PF	TS-0068A Sublot	Gel melted on some capsules, some leakers 3/60 leakers	Gel melted. 1/60 leakers	Some capsules were deformed. Capsules were not oily. Only one capsule was found with melted spot on the side of the capsule. No leakers were found.	Pass. No leakers were found.	Pass. No leakers were found.

Trial #1 Vit E

Trial #2 Vit E

Trial #3 Fish

Trial #4 Lecithin

Main + Sublot equivalent

Main + Sublot equivalent

Main + Sublot equivalent

Sublot superior to main lot

* some recycled gel mass used for fish sublot 5b7 and lecithin main lot 68 ; 4th recycled gel mass used for lecithin sublot 6B7 which shows no leakers and no deformity

* results are not consistent from no 1 - 2 - 3 physical results